

Cosmetic Products and Their Current European Regulatory Framework

1. Cosmetic Products and Their Current European Regulatory Framework

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1.1 Introduction

Although Dir. 76/768/EEC relating to cosmetic products [EU, 1976b] is a vertical legislation and every cosmetic product placed on the European market must fulfil its requirements, it would be very unrealistic to assume that this is a stand-alone piece of legislation that is not affected by other legal texts. In practice, Dir. 76/768/EEC forms part of a complex legislative process that was initiated more than 40 years ago to guarantee the free movement of goods within Europe while simultaneously ensuring the safety of the European citizens and their environment. The major milestones in this process are depicted in figure 1.

The current chapter provides an overview of the most relevant features of the Cosmetic Products Directive, which in fact forms the basis of this book. Thereafter, the milestones depicted in figure 1 are individually discussed in the light of their relevance to the cosmetic regulatory framework.

1.2 The Cosmetic Products Directive

1.2.1. Definition of a Cosmetic Product

According to the European Commission Dir. 93/35/EEC, Art. 1, a cosmetic product is defined as ‘any substance or preparation intended to be placed in contact with the various parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odours and/or protecting them or keeping them in good condition’ [EU, 1993a]. This definition gives an indication on the target site of application of a cosmetic product and on its allowed functions [Colipa, 2004]. Thus, products such as skin creams, lotions, perfumes, lipsticks, fingernail polishes, eye and facial make-up preparations, soap products, shampoos, permanent waves, hair colours, toothpastes, deodorants, ... fall under the category of cosmetic products in the EU. More questionable product types such as suntanning preparations, antiperspirants and antidandruff shampoos are also considered cosmetics within Europe, whereas this may differ in other parts of the world [Pauwels and Rogiers, 2004].

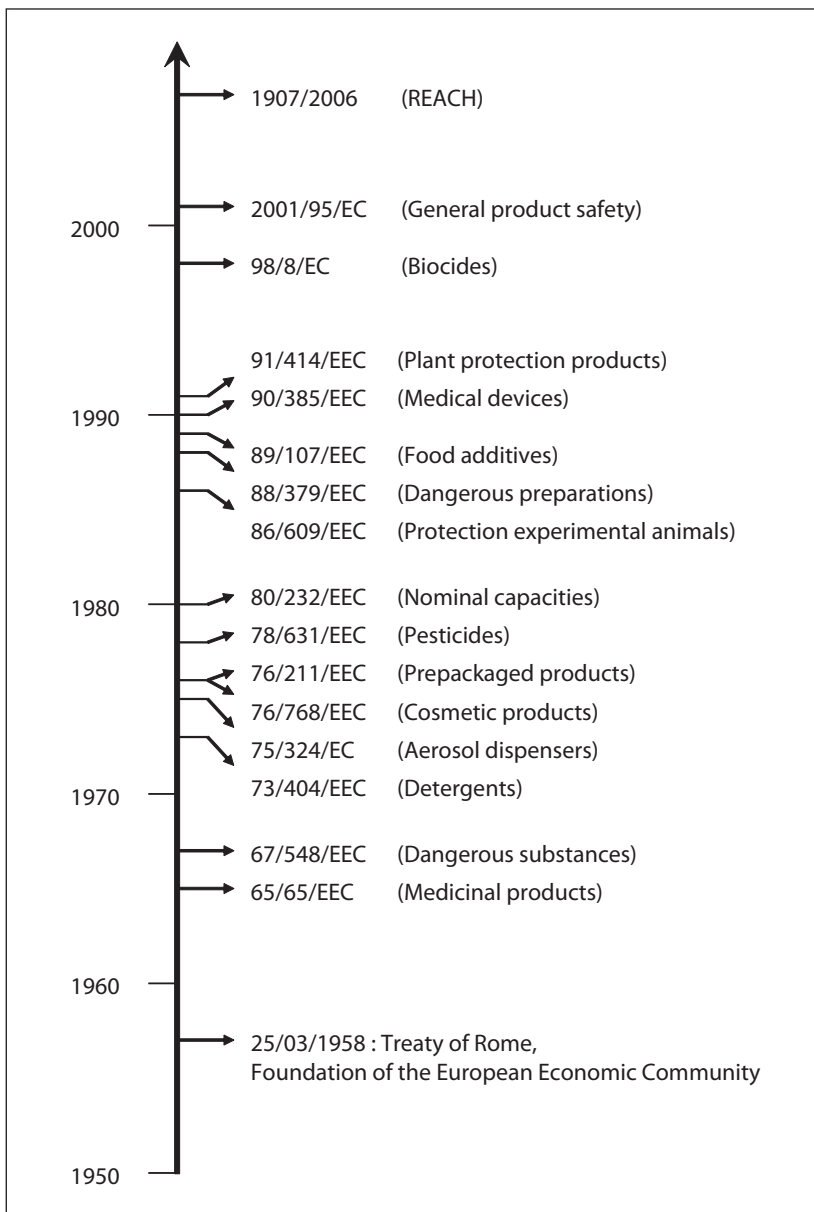


Fig. 1. Overview of the major milestones in the EU chemical-related legislative process.

1.2.2. The Safety Prerequisite and Responsibilities

The current EU legislation on cosmetics literally states that ‘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 account, in

particular, of 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' (Art. 2). The responsibility to ensure that cosmetic products are safe for consumer use is placed upon the manufacturer or his authorised agent or any other person responsible for placing the product on the Community market [EU, 1993a].

A qualified safety assessor, holding a specified diploma [EU, 1989b] in the field of pharmacy, toxicology, dermatology, medicine or a similar discipline, undersigns the safety assessment of the cosmetic product under consideration and thus takes responsibility for the safety of the product when applied under reasonably foreseeable conditions of use.

By means of a post-marketing surveillance system, the EU Member States are on their turn expected to take all necessary measures to ensure that only cosmetic products which conform to the provisions of Dir. 76/768/EEC and its Annexes may be placed on the European market (Art. 3) [EU, 1993a]. Nevertheless, the ultimate responsibility for the safety of a cosmetic product resides with industry.

1.2.3. The Public Information Prerequisite

In order to optimally inform the consumer, every cosmetic product sold in the EU must contain the following information on its label (Art. 6):

- a name and address of manufacturer or responsible for placing on the market within the EU,
- b nominal content of the finished product at the time of packaging (weight or volume),
- c date of minimal durability (products with a minimum durability less than 30 months) or an indication of the period of time after opening for which the product can be used without any harm to the consumer,
- d particular precautions to be observed in use, especially those indicated in the Annexes to Dir. 76/768/EEC,
- e batch number, enabling identification of manufacturing,
- f function of the product, unless evident,
- g a list of ingredients in INCI in descending order of weight at the time they were added, unless they are present at a concentration below 1%, in which case they may be mentioned in any chosen order.

Moreover, the qualitative and quantitative composition of the cosmetic and the existing data on undesirable effects on human health resulting from use of the cosmetic product are enforced to be made easily accessible to the public by any appropriate means, including electronic means. Whereas the qualitative composition already features on the label (ingredient list mandatory), the quantitative composition is limited to 'dangerous substances' according to Dir. 67/548/EEC (see section 1.4.1).

1.2.4. The 'Technical Information File' Prerequisite

For cosmetic products, the EU legislation does not foresee an extensive pre-marketing notification/authorisation procedure involving a full toxicological dossier on the ingredients and the finished cosmetic product. Instead the EU Member States are charged with the installation of a post-marketing surveillance system to check industry's compliance with the provisions of the Cosmetic Products Directive.

To this respect, Art. 7a of the Cosmetic Products Directive imposes that the following information should be readily accessible to the Member States' Competent Authorities [EU, 1993a, 2003]:

- a the qualitative and quantitative composition of the product,
- b physicochemistry, microbiology and purity of the ingredients and the cosmetic product,
- c the manufacturing method,
- d safety assessment of the finished cosmetic product,
- e name and address of the safety assessor,
- f existing data on undesirable effects on human health,
- g proof of the effects claimed,
- h data on animal testing.

The compilation of points a–h is commonly referred to as a cosmetic's TIF or PIR.

1.2.5. The Annexes to the Cosmetic Products Directive and the SCC(NF)P

Like the majority of EU Directives, Dir. 76/768/EEC is composed of the classical set of articles (definitions, responsibilities of the EU Member States, safeguard clause, ...), followed by a number of technical annexes. Five of them consist of ingredient lists:

- Annex II: list of forbidden substances in cosmetic products.
- Annex III: list of substances which are not allowed to be used in cosmetic products outside the restrictions and conditions laid down.
- Annexes IV, VI and VII: lists of allowed colorants, preservatives and UV filters, respectively, accompanied by their maximum levels and/or conditions of use in cosmetic products.

The content of the Annexes is regularly updated through amendments or adaptations to technical progress of the Cosmetics Directive. The cosmetic legislation charges the EU Member States with the designation of a competent authority responsible for checking that every cosmetic product's composition complies with the provisions laid down in the above Annexes [Art. 4; EU, 1993a].

For the safety assessment of the ingredients appearing on the Annexes, the Commission is assisted by the SCCP, previously called the SCCNFP. The SCCP forms part of DG SANCO and owns the official mandate to provide opinions on questions concerning the safety of consumer products (non-food products intended for the

consumer). It is composed of independent scientists in the field of medicine, toxicology, pharmacy, dermatology, biology, chemistry, and other disciplines, collectively covering a wide range of expertise for this multidisciplinary committee [SCCP, 2006]. Together with the SCHER and the SCENIHR, the SCCP provides the Commission with sound scientific advice needed when preparing policy and proposals relating to consumer safety, public health and the environment. In addition, the ICCG, consisting of the chairs and vice-chairs of SCCP, SCHER and SCENIHR, warrants harmonisation of risk assessment and deals with questions which are common to more than one Committee, diverging scientific opinions and exchange of information on the activities of the three Committees¹.

The SCCP specifically addresses questions in relation to the safety and allergenic properties of cosmetic products and ingredients with respect to their impact on consumer health, toys, textiles, clothing, personal care products, domestic products such as detergents, and consumer services such as tattooing [SCCP, 2006; EU, 2004a]. In this context, the committee also performs full risk assessments for candidate ingredients to be included in the Annexes to the Cosmetic Products Directive. The SCCP is not responsible for the safety assessment of cosmetic ingredients not taken up in the Annexes to the Cosmetic Products Directive [SCCP, 2006].

Since 1997, the opinions of the SCCP and SCCNFP are made publicly available through the Committees' websites².

1.2.6. The Animal Testing Ban for Cosmetics and Their Ingredients

Since the cosmetic field is often seen as a luxury area, posing no health benefits, being innocuous and not needing any innovation, it turned out to be a fruitful battlefield for animal protection organisations, politicians and Parliament lobbyists to introduce an animal testing ban. Although it was clear from the start that only a limited number of animals could be saved by banning animal tests for the safety of cosmetics and their ingredients [EU, 2007b], the 'cosmetics case' became a remarkable example of how to introduce alternative methods into legislation in a politically driven and not scientifically driven way. The Sixth Amendment to the Cosmetic Products Directive for the first time introduced the concept of an animal testing ban on cosmetics and their ingredients. More specifically, its Art. 4(1) stated that cosmetic products should not contain 'ingredients or combinations of ingredients tested on animals after 1 January 1998 in order to meet the requirements of this Directive.' This statement was

1 http://ec.europa.eu/health/ph_risk/committees/committees_en.htm (consulted November 2007).

2 http://ec.europa.eu/health/ph_risk/committees/sccp/sccp_opinions_en.htm, http://ec.europa.eu/health/ph_risk/committees/04_sccp/sccp_opinions_en.htm, and http://ec.europa.eu/health/ph_risk/committees/sccp/sccp_opinions_en.htm (consulted November 2007).

somewhat mitigated by the provision that ‘if there has been insufficient progress in developing satisfactory methods to replace animal testing, . . . , the Commission shall, by 1 January 1997, submit draft measures to postpone the date of implementation of this provision, for a sufficient period, and in any case for no less than two years, . . .’ [EU, 1993a]. The mentioned date of implementation was postponed twice [EU, 1997, 2000].

Nevertheless, as a result of the limited progress in alternative method development and with the clear aim of pursuing the abolishment of animal testing for cosmetic products, the 7th Amendment [EU, 2003] to Dir. 76/768/EEC introduced explicit marketing and testing ban provisions for cosmetic products and their ingredients. More specifically, from 11 September 2004 onwards, animal experiments with finished cosmetic products are subject to an absolute ban, whereas a testing ban on ingredients or combinations of ingredients applies step by step as soon as alternative methods are validated and adopted, but with a maximum cut-off date of 11 March 2009, irrespective of the availability of alternative non-animal tests.

In addition, a marketing ban applies step by step as soon as alternative methods are validated and adopted in EU legislation. This marketing ban will be introduced at the latest on 11 March 2009, for all human health effects with the exception of repeated-dose toxicity, reproductive toxicity and toxicokinetics. For these specific health effects, the deadline of 11 March 2013 is put forward, irrespective of the availability of alternative non-animal tests.

More details on the actual status of alternative methods and future prospects can be found in section 3.2.1 and chapter 6.

1.2.7. Safety Assessment of Cosmetic Ingredients under the Cosmetic Products Directive

According to the actual cosmetic legislation in the EU, two distinct channels are operative for the safety evaluation of cosmetic ingredients (fig. 2), namely:

- (i) The safety evaluation of cosmetic ingredients of direct relevance to Council Directive 76/768/EEC, thus substances to be taken up in the Directive’s Annexes IV, VI, VII, III or II being colourants, preservatives, UV filters, substances for which restrictions in application and/or concentration apply, or which end up forbidden, respectively. For these compounds, concern for human health has been expressed [Pauwels and Rogiers, 2004]. They are subject to an evaluation by the SCCP, previously by the SCCNFP. When the outcome is favourable, a substance can be taken up in its corresponding Annex to the Directive [EU, 1976b]. In case the opinion is unfavourable, industry usually is asked to provide additional information and/or argumentation. The final decision on the inclusion lies with the European Directorate General Enterprise. As stated earlier, full reports of SCC(NF)P evaluations, including data with respect to the performed physico-

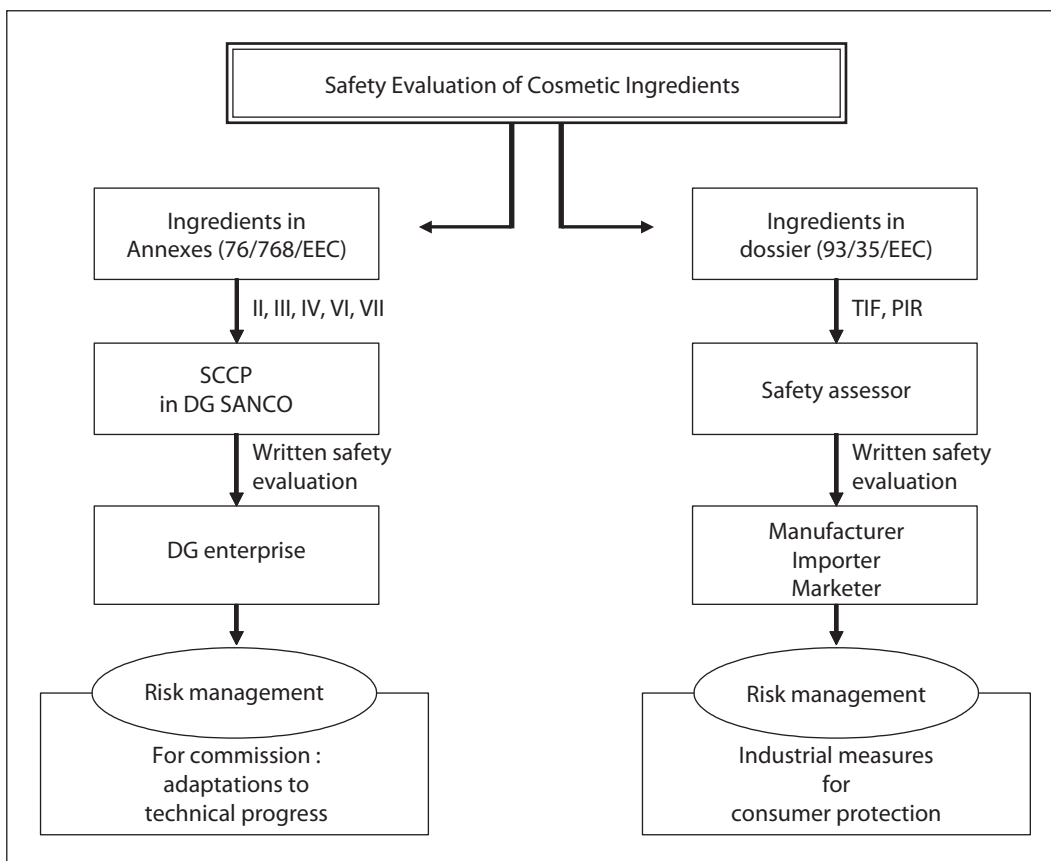


Fig. 2. Existing two ways in the safety evaluation of cosmetic ingredients in the EU [SCCP, 2006].

chemical and toxicological studies with their flaws and strengths, are publicly available through the Internet³.

- (ii) The safety evaluation of all ingredients present in finished cosmetic products. The latter constitutes relevant information for the toxicological data compilation of the cosmetic product under consideration (TIF or PIR). According to Art. 7.a.1.(e) of the 6th Amendment to the cosmetic legislation [EU, 1993a], the safety evaluation needs to be carried out by a qualified safety assessor, whereas the ultimate responsibility for the finished product lies with the manufacturer, importer or marketer. For substances not taken up in one of the Annexes to Dir. 76/768/EEC [EU, 1976b], no specific additional data requirements apply. This means that, besides the results of the safety tests that are carried out on a voluntary basis for certain cosmetic ingredients, the availability of data depends on data requirements

³ http://ec.europa.eu/health/ph_risk/committees/04_sccp/sccp_opinions_en.htm and http://ec.europa.eu/health/ph_risk/committees/sccp/sccp_opinions_en.htm (consulted July 2007).

and data accessibility measures laid down in the other legislation(s) with which these substances have to comply.

In the SCCP 'Notes of Guidance' [SCCP, 2006], a list of the data requirements applicable to the substances taken up in the Annexes of Directive 76/768/EEC [EU, 1976b] is present. It consists of acute toxicity, skin and eye irritation, skin sensitisation, repeated dose toxicity, mutagenicity, reproductive toxicity, carcinogenicity, dermal absorption, toxicokinetics, photo-induced toxicity and human data. Although not every ingredient taken up in a TIF/PIR will benefit of the presence of such a comprehensive toxicological data package, the main principles of hazard and risk assessment, as proposed by the SCCP still can be applied. They are in line with the European Technical Guidance Document on Risk Assessment of the European Chemicals Bureau [ECB, 2003], supplemented with the comments of the SCHER [SCHER, 2005]. The latter clearly highlight the importance of expert judgment in case the data packages are reduced and/or of poor quality.

The general safety assessment paradigm as employed in the cosmetic field will be discussed in section 2.2 and the specific risk assessment of cosmetic ingredients reappears in chapters 3 and 4.

1.2.8. Proposal for a Recast of the Cosmetic Products Directive

Quite recently, the European Commission published a proposal for a Regulation on cosmetic products [EU, 2008], the so-called recast of the 32-year-old Cosmetic Products Directive [EU, 1976b]. This recast is meant to bring together the original directive with all its amendments, simultaneously introducing some substantive changes to the individual texts when incorporated. Since the recast is at the Commission proposal stage, it requires extensive discussions between the Member States and within the European Parliament, implying that it will not remain unchanged. Nevertheless, it is useful to provide an overview of the major changes that are currently introduced. It should, however, be noted that the list below is not exhaustive and that it cannot be foreseen which of the provisions will actually be taken up in the final version of the regulation.

a) Moving from a Directive to a Regulation

One of the main goals for the recast being simplification of the administrative procedures related to the Cosmetic Products Directive, the text proposed aims at becoming a 'Regulation on cosmetics'. European regulations have the advantage that they are binding in their entirety and directly applicable in all Member States, whereas directives need to be transposed into the national legal frameworks of the individual Member States. To demonstrate the complexity of this process, the transposition of Dir. 76/768/EEC into Belgian law is worked out in appendix 1. With the 27 Member States Europe currently counts, regulations automatically represent a major administrative simplification for the Member States.

The articles of the original directive have been reorganised into chapters displayed in a logical order.

b) Introduction of a Set of Definitions

The recast aims at clarifying a number of issues for which legal uncertainty exists. Therefore, definitions for terms such as ‘manufacturer’, ‘importer’, ‘placing on the market’, ‘making available on the market’, ‘harmonised standard’, ‘traces’, ‘preservatives’, ‘colourants’, ‘UV-filters’, ‘(serious) undesirable effect’, ‘repeal’ and ‘withdrawal’ are introduced in Art. 2 and some definitions of different cosmetic product types, such as ‘rinse-off product’, ‘leave-on product’, ‘hair product’, ‘skin product’, etc. are included in a preamble to Annexes II–VI. This preamble would replace the original Annex I to the Cosmetic Products Directive [EU, 1976b], which contains a non-exhaustive list of possible cosmetic product types.

c) One Single European Notification and a Strengthened Market Control

The proposed recast introduces a single centralised electronic notification of certain information concerning the product placed on the market. Instead of having to notify in every individual Member State and needing to comply with all the national provisions (e.g. communication to poison control centres), the recast now foresees one single notification and one single poison control communication at the European level.

The Member States are responsible for in-market control and in case of non-compliance, some specific possibilities for actions to be taken are mentioned in the recast (e.g. the introduction of penalties).

d) New Provisions for CMR Substances

Substances classified as CMR Category 1 or 2 according to the principles of Directive 67/548/EEC [EU, 1967], are actually prohibited for use in cosmetic products [EU, 2003]. The basic principle would remain unchanged, but the recast opens more possibilities in the sense that *there should be a possibility, in the exceptional case where these substances are legally used in food and no suitable alternative substances exist, to use such substances in cosmetic products if such use has been found safe by the SCCP.*

e) Introduction of Harmonised Standards

Throughout the text, reference is made to the use of ‘harmonised standards’. This implies that the Commission considers further development of European standards for analytical methods, claim substantiation, etc., enabling insurance of product compliance in these fields.

f) Clarifications on the Safety Assessment of Cosmetic Products

The TIF or PI(F) would be called the ‘Cosmetic Safety Report’. A newly created Annex I to the regulation would contain some guidance on the content of this report.

A responsible person ensuring that the cosmetic safety report is kept up to date is to be designated.

The qualifications of the safety assessor are specified within the text and allow safety assessors from outside Europe to sign the cosmetic product safety assessment.

g) 'INCI' Becomes 'Name of Common Ingredients Glossary'

The recast replaces the original INCI list by the so-called 'Common Ingredients glossary'. This glossary is described to contain the names of relevant cosmetic ingredients (approximately 10,000), but not to constitute a list of authorised cosmetic ingredients. This is the same definition as was given for the INCI list, meaning that only the name has changed.

Viewing the preliminary stage of this new 'Regulation on cosmetics', its detailed content is not further taken up in this chapter. The final regulation is not expected before 2009.

The only certainty seems to be that all statements related to the animal testing ban as mentioned in the current cosmetic legislation [EU, 2003] are precluded to be changed.

1.3 Relevant 'Vertical' EU Legislations

In parallel to the Cosmetic Products Directive, some other important legal milestones deal with the protection of human health against specific types of substances. These so-called 'vertical' legislations are depicted in figure 3.

Since the current European legal context prohibits testing of finished cosmetic products on experimental animals, the impact of the above-mentioned Directives will individually be discussed with special focus on toxicological data generation and data availability potentially relevant for the safety assessment of cosmetic ingredients.

When compiling all the knowledge on data generation and data availability through the different legislations, it is in certain cases possible to foresee the type and amount of toxicological data one can expect to find on a particular cosmetic ingredient.

1.3.1. Impact of the Dangerous Substances Directive and REACH

a) General Provisions

Over the past four decades, chemical substances have been regulated at the European level by Dir. 67/548/EEC [EU, 1967], its amendments and adaptations to technical progress. In first instance, this chemical legislation covered the listing and review of existing substances in the EU, together with the notification of new chemicals. Basically, a new chemical substance could only be produced within or imported into

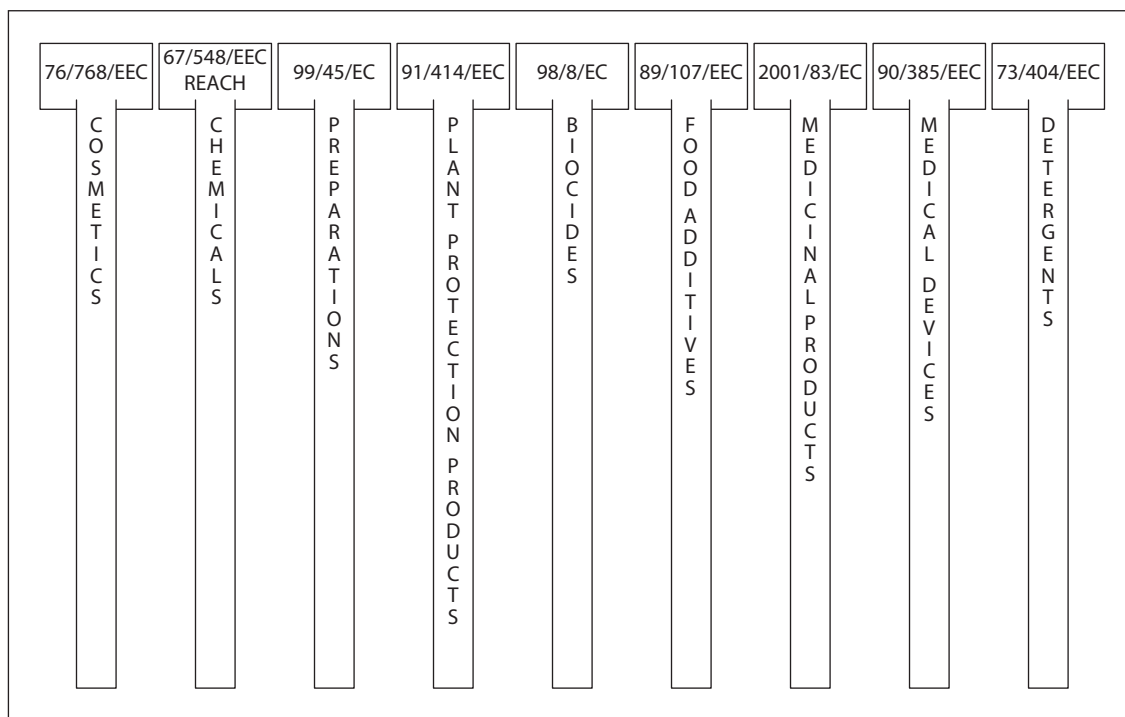


Fig. 3. Schematic presentation of 'vertical' cosmetic-related legislations in the EU.

the EU after having received a favourable judgment from the EU Member State's competent authority to which a full notification dossier has been addressed.

In a second stage, the Dangerous Substances Directive laid down the rules for classification and labelling of chemical substances in the EU. This means that not only test descriptions for physicochemical (Annex V, Part A), toxicological (Annex V, Part B) and ecotoxicological (Annex V, Part C) studies were provided, but also some explicit rules to translate the results from physicochemical and/or (eco)toxicological studies into a classification involving appropriate risk and safety phrases to be mentioned on the label (Annex VI). The classification and labelling principles of Directive 67/548/EEC are still referred to in many other EU legislative texts.

The recently published EU Regulation No. 1907/2006 [EU, 2006a] concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals, commonly referred to as 'REACH', introduces some major changes in the EU regulatory framework for chemicals, among which:

- The reversal of the burden of proof: manufacturers and/or importers become fully responsible for proving and ensuring that their substances are safe to use, whereas previously the Member States' competent authorities equally expressed an approval for the safe use of the substance under consideration [Recitals 18, 25, 29, Art. 4; EU, 2006a].

- The creation of a European Chemicals Agency, established for the purposes of managing and in some cases carrying out the technical, scientific and administrative aspects of REACH and to ensure consistency at Community level in relation to these aspects [Art. 75; EU, 2006a].
- Protection of experimental animals: REACH intends to reduce testing on vertebrate animals as much as possible by imposing data sharing, by prohibiting duplication of animal testing, and by the promotion of 3R⁴-alternative methods [Recitals 1, 33, 37, 40, 47, 49, Art. 13(2), 15, 25, 26(3), 27, Annex VI(1.4)]. Moreover, for the highest tonnage levels (>100 tonnes/year), testing proposals need to be officially approved before the animal experiments are initiated [Recital 64, Art. 22(1h), 40; EU, 2006a].
- ‘PBT’, ‘vPvB’, ‘CMR’ substances and the substitution principle: REACH describes specific procedures as well for environmentally PBT and vPvB substances, as for CMR substances [Art. 14(4), 40(1), 58(3)]. Moreover, every application for authorisation for such a substance must include an analysis of possible substitute substances or procedures as well as an analysis of their technical and economic feasibility [Recitals 12, 70, 72, Art. 55; EU, 2006a].
- Enforcement of restrictions: prohibitions on substances or restrictions on certain uses were previously imposed through Dir. 76/769/EEC [EU, 1976c], its amendments and numerous adaptations to technical progress. They will now be taken up by REACH through a faster and simplified procedure [Recitals 23, 80, 84, 85, Art. 68; EU, 2006a].
- The flow of information up and down the supply chain: suppliers of a substance or a preparation must provide to their customers a safety data sheet including as well information about any potential hazard as detailed exposure scenarios. In order to enable suppliers to draw up correct exposure scenarios, downstream users will need to ensure a good upstream communication on potential usage patterns [Recital 56, Art. 31, 32, 37, 38; EU, 2006a].

b) Relevance for Cosmetics

Although most cosmetic ingredients by definition are chemicals [EU, 1992], they are exempted from the classification, packaging and labelling provisions of the Dangerous Substances legislation and REACH. It remains, however, quite informative to consult it. For example, knowing whether the substance under consideration is taken up in one of the official chemical inventories (EINECS or ELINCS), already gives an indication on the amount of available data.

Indeed, EINECS lists and defines those chemical substances deemed to be on the European market between 1 January 1971 and 18 September 1981, the so-called ‘existing’ chemical substances. EINECS is a closed list containing about 100,000 substances, excluding polymers. For the majority of chemicals on EINECS, the amount of available information is limited.

4 Refinement, Reduction and Replacement.

Table 1. Summary of data requirements for notified chemical substances according to Dir. 92/32/EEC [EU, 1992]; exemptions, cumulative volume requirements or other exceptions are not mentioned

10–100 kg/year	100 kg to 1 tonne/year	1–10 tonnes/year 'Base set'	>10 tonnes/year
acute toxicity	acute toxicity skin irritation eye irritation skin sensitisation mutagenicity	acute toxicity skin irritation eye irritation skin sensitisation mutagenicity subacute toxicity (28 d) toxicokinetics screening reproduction toxicity	acute toxicity skin irritation eye irritation skin sensitisation mutagenicity subacute toxicity (28 d/90 d) toxicokinetics screening reproduction toxicity reproduction toxicity carcinogenicity metabolism studies

ELINCS on the other hand, is an open list, containing per definition all substances not taken up in EINECS, unless they are polymers. As summarised in table 1, these so-called 'new' chemical substances are subject to data requirements triggered by the annual volumes in which they are produced within or imported into the EU [EU, 1992]. However, the repeated dose and reproductive toxicity data, as mentioned in the last column of the table (>10 tonnes/year), are only mandatory upon specific request by the competent authorities, based upon the outcome of previous testing.

All the study results and summaries are considered non-confidential [EU, 1992] and supplement the information figuring on the chemical's label and MSDS.

As stated earlier, the existing EU notification system for chemicals is in the process of being replaced by a set of new rules and procedures (including new sets of data requirements) through EU Regulation No. 1907/2006 [EU, 2006a], commonly referred to as 'REACH'.

REACH intends to bring the data requirements for existing and new chemical substances to the same level and therefore introduces tonnage-linked data requirements for existing substances.

Therefore, the latter are expected to display an overall increase in available toxicological data. As far as the new chemical substances are concerned, the data packages are reduced compared to the requirements defined in Dir. 92/32/EEC, e.g. the so-called 'Base Set' shifted from 1 to 10 tonnes [EU, 1992] to the >10 tonnes level [EU, 2006a].

The introduction of alternative approaches to animal testing under REACH is expected to significantly impact the type and amount of available toxicological data.

Nevertheless, the extent of this impact will depend on the policy followed by ECHA and by the level of acceptance by the European competent authorities of those alternative approaches. Since REACH only recently entered into force (June 2007), the data collection under this new legislation is only in a preparatory phase.

Another important feature introduced by REACH consists of a number of duties of downstream users of chemicals, including the cosmetic industry. According to the Regulation [EU, 2006a], all supported existing chemicals need to be pre-registered between the 1st of June and the 1st of December 2008. Subsequently, the Commission will, by the 1st of January 2009, publish a list of those chemicals. Downstream users should carefully check this list to see whether all cosmetic ingredients in which they are particularly interested figure on it and are accompanied by the 'correct' use. Moreover, downstream users have the obligation to report information up the supply chain and, in some cases, compilation of own chemical safety reports is necessary. On their turn, the suppliers/manufacturers have the duty to communicate down the supply chain a minimal information package for those substances or preparations for which a safety data sheet is not required. This already applies from 1 June 2007 onwards. The MSDS itself is also reviewed and will provide more detailed toxicological information together with the inclusion of an annex on the identified uses and exposure scenarios of the substance/preparation under consideration [EU, 2006a].

1.3.2. Impact of the Dangerous Preparations Directive

a) General Provisions

As early as 1973 and 1977, solvents, paints, varnishes, printing inks, adhesives and similar products were identified as requiring special attention, and thus rules on these categories of preparations were laid down [EU, 1973a, 1977]. However, divergences in national legislations on the remaining types of preparations still constituted a significant barrier to trade within the EU and led to the publication of an overall Dangerous Preparations Directive [EU, 1988, 1999b].

b) Relevance for Cosmetics

Since 'preparations' are defined as *mixtures or solutions composed of one or more substances* [EU, 1999b], numerous cosmetic ingredients fall under this category.

Although cosmetics are exempted from its packaging, classification and labelling provisions, Dir. 99/45/EEC [EU, 1999b], replacing 88/379/EEC [EU, 1988], contains a number of features of interest for the data availability on cosmetic ingredients. When purchasing a preparation for use as a cosmetic ingredient, it is useful to know that a preparation containing one or more constituents classified in a danger class is not necessarily considered dangerous in its marketed form. The legislation leaves it up to the marketer to either subject the mixture to extensive toxicological and ecotoxicological testing, or to use the so-called 'conventional method'. The latter represents a conservative

calculation combining the hazardous properties of the classified constituent with its final concentration in the preparation under study. For example, a simple aqueous formulation containing more than 20% of a compound classified as irritating to the skin, would automatically be classified as irritating to the skin without further testing. Viewing the ethical concerns in the EU with regard to animal testing, the conventional method is abundantly applied for the classification of dangerous preparations.

This means that in the majority of cases, no toxicological data on mixtures of chemicals were generated. In view of evaluating the safe use of a 'preparation' in a finished cosmetic product, having access to its quantitative composition is crucial. Dir. 99/45/EC [EU, 1999b], however, does not impose disclosure of all details. In several cases, it may be legal that the label and accompanying documents, including the MSDS, do not reveal the full composition of a (dangerous) preparation in the EU.

1.3.3. EU Legislation on Food Additives

a) General Provisions

Since food additives are intended to be ingested, this type of chemicals calls for a separate set of legal provisions and a risk assessment procedure. In Europe, food additives are regulated through a number of complementary Directives [EU, 1989a, 1994a, b, 1995], based upon the common principle that only those additives that are explicitly authorised and taken up in the official EU positive lists may be used and only subject to the specific restrictions laid down.

In 2002, after a number of serious food crises in Europe (bovine spongiform encephalopathy, dioxins, acrylamide), the general principles and requirements of food law were translated into a new Regulation [EU, 2002]. The EFSA was established to produce scientific opinions and advice for drawing European policies and legislation (inter alia the adaptations to the positive lists) and to support the European Commission, European Parliament and EU Member States in taking effective and timely risk management decisions with regard to food and food additives.

b) Relevance for Cosmetics

In general, an officially accepted food additive has been subject to a full risk assessment allowing calculation of the ADI by making use of the outcome of a full toxicological dossier consisting of acute and repeated dose toxicity studies. This exercise is currently performed by the EFSA Scientific Panel on food additives, flavourings, processing aids and materials in contact with food. The relevant opinions can be downloaded from the Internet⁵.

⁵ http://www.efsa.europa.eu/en/science/afc/afc_opinions.html (consulted July 2007).

As a consequence, the cosmetic ingredients that are also accepted as food additives in the EU may have the benefit of a large data package of which the summary is freely available through the EFSA Website. Moreover, these ingredients are safe for daily ingestion up to a specific level, which often makes them ideal candidates to be used in cosmetic products at comparable exposure levels.

1.3.4. Impact of the Biocidal Products Directive

a) General Provisions

Since biocidal active substances are intended to kill living organisms, they need to be accurately classified, labelled and controlled in order to inform and protect the professional user and/or the general public. Therefore, the Biocidal Products Directive [EU, 1998] deals with data requirements and risk assessments of active substances and ready-to-use end products. Herein, the classification and labelling provisions of the Dangerous Chemicals and Preparations Directives are taken over.

b) Relevance for Cosmetics

Dir. 98/8/EC [EU, 1998] covers the placing on the market of 23 biocidal product types, currently existing in the EU. Active substances need to be approved and officially listed before they may be used. Not only their ecotoxicological and toxicological profiles need to be examined, but also their efficacy and avoidance of resistance of the organisms they are intended to counteract. The content of a typical toxicological dossier for a biocidal active substance consists of acute toxicity, skin and eye irritation, skin sensitisation, subacute and subchronic toxicity, mutagenicity and teratogenicity. Unless justification is given for not performing the tests, chronic toxicity, carcinogenicity and two-generation reproductive toxicity complete the data package. These data are not considered to be confidential information [EU, 1998].

The intersection between biocidal active substances and cosmetic ingredients mainly consists of preservatives used in cosmetics. These are substances taken up in Annex VI to the Cosmetic Products Directive [EU, 1976b]. The data packages generated under the Biocidal Products Directive may contain some additional useful data on these preservatives and therefore their summaries may be helpful to consult. Also data on the potential development of resistance may be of use.

1.3.5. Impact of the Medicinal Products Directive

a) General Provisions

The first version of a directive regulating the marketing of medicinal products in the EU was issued in 1965 [EU, 1965]. It has been repeatedly adapted and finally replaced by its current version in 2001 [EU, 2001a], significantly amended in 2004 [EU,

2004b]. The combination of the uncontested benefit and social value of medicines on the one hand and their potential side effects on the other hand, leads to the necessity of extensive regulatory requirements.

Full toxicological and clinical dossiers are presented to the Member States' competent authorities, and active medicinal substances are approved under the wings of the EMEA.

b) Relevance for Cosmetics

As the Medicinal Products Directive [EU, 1965, replaced by EU, 2001a] regulates chemicals intended to exert a pharmacological, immunological or metabolic action in the human body, the regulatory data requirements for their safety assessment are extensive. A new drug application consists of a comprehensive quality section, a non-clinical (in vitro tests and animal experiments) part and finally, an extensive clinical part, involving the use of groups of human volunteers and patients. The non-clinical test results include single and repeated dose toxicity, toxicokinetics, genotoxicity, carcinogenicity, reproductive and developmental toxicity and local tolerance [EMEA, 2006]. Knowledge on data accessibility for active medicinal substances involves insight in a complex web of data protection measures in order to safeguard the commercial property of the companies that have invested in such elaborated and costly quality, efficacy and safety dossiers [EU, 1993c]. Nevertheless, some data can be accessed when compounds come off patent protection and/or from the scientific press.

In the EU, the use of medicinal active substances in cosmetics is strongly discouraged. Many medicinal actives are taken up in Annex II to the Cosmetic Products Directive, meaning that their use in cosmetics is prohibited. A number of exceptions exist, but as a general rule, the intersection between active medicinal substances and ingredients allowed in cosmetics, is very restricted.

1.3.6. Impact of the EU Legislation on Detergents

a) General Provisions

Viewing their chemical nature (many are anionic surfactants), the primary objective of the EU regulator was to protect the environment by stipulating a minimal level of surfactant biodegradability [EU, 1973b]. Subsequently, the legislation on detergents has been amended on several occasions until it was published in its final form in 2004 [EU, 2004c]. Again, the focus was maintained on environmental aspects, although human local health effects were also taken into consideration.

b) Relevance for Cosmetics

Cleansing cosmetic products typically contain different kinds of surfactants which also form part of detergents. Human safety appearing to be of inferior importance in the assessment of these types of ingredients, only local health effects such as allergenicity and skin irritation, are addressed. Moreover, the only official data requirements

involve labelling of known allergens, thus usually no new data are generated. This strongly reduces the impact of the Detergents Directive on the safety data availability of cosmetic ingredients.

1.3.7. Impact of the Plant Protection Directive and the EU Legislations on Medical Devices

a) General Provisions

- (i) As was the case for biocides, plant protection active substances kill living organisms, wherefore they need to be thoroughly assessed. Moreover, the actives may be found as residues on treated crops, implying that the available toxicological data should enable the calculation of an acceptable daily intake. Therefore, the EU Plant Protection Products Directive [EU, 1991a] deals with the extended data requirements and risk and efficacy assessments of active substances and ready-to-use end products.
- (ii) In the medical field, not only medicinal products, but also a large number of instruments and high-tech devices are used for performing very specific examinations. The first regulation in this particular field dealt with active implantable medical devices [EU, 1990]. Three years later, the whole area was covered by a new Directive [EU, 1993b] which clearly defined all possible classes of medical devices together with their data requirements and further regulatory demands.

b) Relevance for Cosmetics

Although extensive toxicological data, of which the results are accessible, are generated through the Plant Protection Products Directive [EU, 1991a], only few to none of them are of relevance for cosmetic products.

The same applies to the data generated through the Medical Devices Directive [EU, 1993b], with the exception that the generated data are considered confidential and therefore not readily accessible [EU, 1993b].

1.3.8. Combined Impact of Relevant 'Vertical' EU Legislations on Data Availability for a Cosmetic Ingredient

In principle, any chemical substance legally marketed in the EU could be a cosmetic ingredient candidate, on the condition that all the restrictions and prohibitions imposed by the EU cosmetic legislation with respect to the different articles, annexes and animal testing, are taken into consideration. This implies that a cosmetic ingredient may have been tested through the requirements of diverging EU Directives, irrespective of its use in a finished cosmetic product. Out of the thousands of ingredients used in cosmetics, less than 400 are taken up in Annexes III to VII of Dir. 76/768/EEC

[SCCP, 2006]. Among these, the majority of preservatives (listed in Annex VI) were equally approved through the biocidal products (and/or plant protection products) legislation and therefore automatically benefited from a large amount of physico-chemical, toxicological and ecotoxicological data.

A number of flavouring agents may equally be used as food additives, meaning that potentially the ADI and a full toxicological profile are available. Moreover, in the area of food contact materials a large number of substances have been evaluated⁶ which could find a use in cosmetics. Several surfactants are applied in detergents, skin care and skin cleansing products and many skin care products contain constituents that are used as excipients in topical medicines.

Yet it is clear that the specific intersection between the pool of dangerous substances and that of cosmetic ingredients not taken up in any Annex will by far be the largest one. The chemicals in that intersection have solely been subject to the data requirements laid down by the Dangerous Substances Directive [EU, 1967]. This means that there are two possibilities with regard to their data availability:

- when listed on ELINCS, the amount of data depends on annual volumes on the market (table 1),
- when listed in EINECS, the expected data package cannot be predicted, but usually is rather limited.

Figure 4 summarises the information provided under the different EU legislations by giving an overview of data availability for different types of substances/preparations. It is a simplified representation since it contains neither non-EU regulatory requirements nor the numerous exceptions mentioned in the individual Directives.

The dermal absorption test does not occur separately in figure 4. Although of key relevance for cosmetic ingredients, dermal absorption data are not commonly generated for other types of substances, with the exception of plant protection products coming in contact with the skin. Consequently, *in vitro* dermal absorption studies, of basic importance for the cosmetic ingredients studied by the SCCP, will rarely if ever be found in data packages generated under legislative requirements outside the cosmetic field.

The current chapter clearly shows that it is quite important to understand the current chemical-related EU regulatory framework, not only to comply with the concerned pieces of legislation, but equally in order to retrieve a maximal amount of safety data on cosmetic ingredients, available through different sources. More specifically, it shows that, although cosmetics on the EU market are exempted from the legislations on dangerous substances, dangerous preparations, food additives, biocides, detergents, medicinal products, plant protection products and medical devices, a lot of useful safety information on cosmetic ingredients may have become available

⁶ http://ec.europa.eu/food/food/chemicalsafety/foodcontact/synoptic_doc_en.pdf (consulted July 2007).

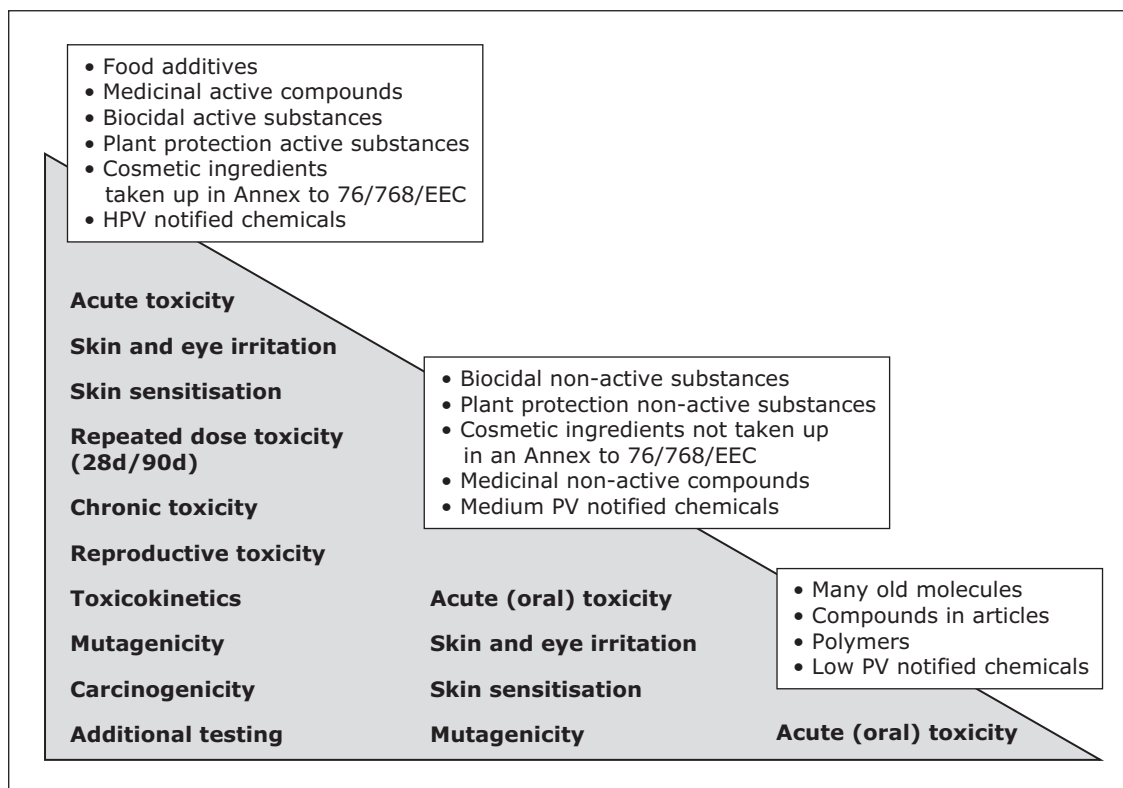


Fig. 4. Schematic representation of expected data availability for different types of substances as a result of current EU regulatory requirements.

through their provisions. Therefore, general knowledge of the chemical-related EU legislation has become indispensable and needs to be continuously updated.

A topic that merits continuing attention is the legislation on dangerous substances and more specifically the new road taken with REACH. Monitoring the implementation and practical realisation of REACH is crucial in maintaining a realistic view on safety data availability for a large number of cosmetic ingredients.

1.4 Relevant 'Horizontal' EU Legislations

Besides the above-mentioned 'vertical legislations' co-existing in the EU, some horizontal directives also affect the regulatory background for cosmetics (as visualised in figure 5). In most cases, they are complementary to the Cosmetic Products Directive, but sometimes their provisions overrule the cosmetic legislation, wherefore they certainly deserve to be mentioned.

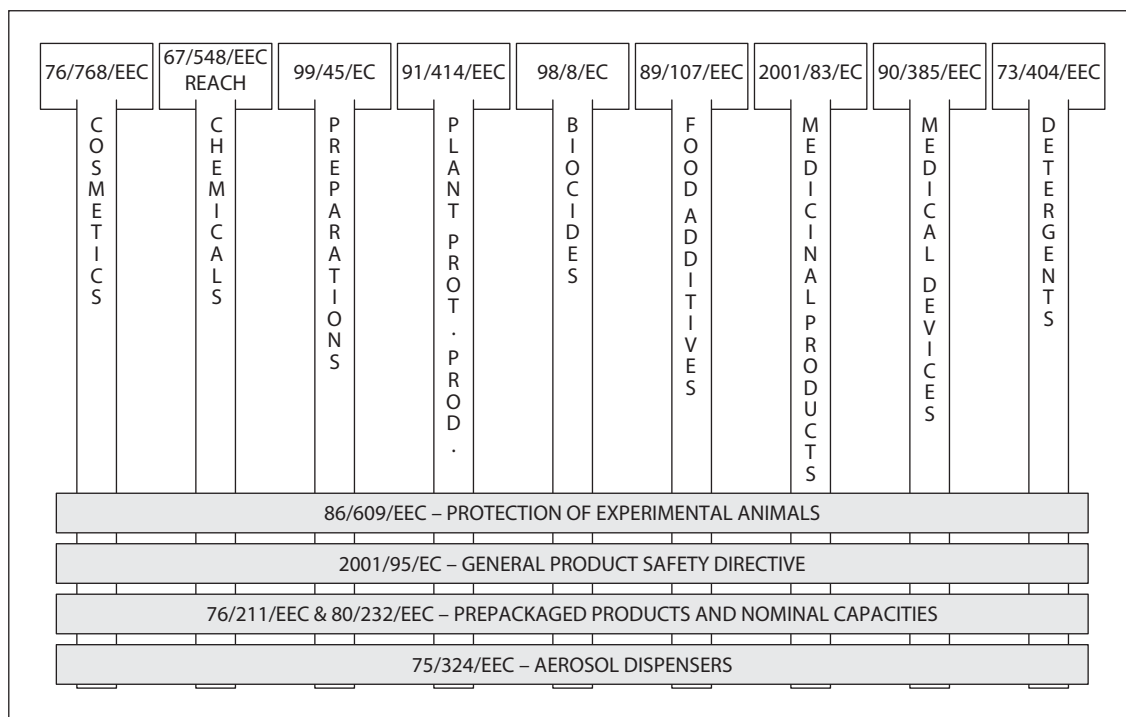


Fig. 5. Schematic presentation of 'vertical' and 'horizontal' cosmetic-related legislations in the EU.

1.4.1. Horizontal Provisions for the Protection of Animals

A Directive commonly referred to by other pieces of legislation is Dir. 86/609/EEC on the protection of animals used for experimental and other scientific purposes [EU, 1986]. Seeking to improve the controls on the use of laboratory animals in nearly all sectors, Dir. 86/609/EEC sets minimum standards for housing and care (Art. 5) and for the training of personnel handling animals and supervising the experiments [Art. 7(1), 14].

It also aims at reducing the numbers of animals used for experiments by requiring that an animal experiment should not be performed when an alternative method exists [Art. 7(2)], and by encouraging the development and validation of alternative methods to replace animal methods [Art. 23(1)]. The latter served as the basis for the Commission to set up the ECVAM [EU, 1991b]. Member States are imposed to collect statistical information on numbers and use of animals in experiments (Art. 13).

It should be emphasised, however, that the scope of Dir. 86/609/EEC is restricted to (1) animal use in the framework of the development, manufacture, quality, effectiveness and safety testing of drugs, foodstuffs and other substances or products, and (2) to the protection of the natural environment in the interest of the health or welfare of man or animal (Art. 3). Thus the fields of scientific research, education and training

and forensic research are not covered by this horizontal directive. Acknowledging this gap and in order to protect animals used in any procedure which may possibly cause pain, suffering, distress or lasting harm, the Council of Europe published Decision 1999/575/EC [EU, 1999a]. Herein, a number of conclusions of the 1986 European Convention for the protection of vertebrate animals used for experimental and other scientific purposes are officially approved. Basically, they defend the same principles as Dir. 86/609/EEC, but they additionally cover the neglected areas.

With the scientific progress made since 1986 and with the increasing political pressure on the development of alternative methods, a revision of Dir. 86/609/EEC was inevitable. Despite years of surveys and discussions on several aspects of the Directive such as scope, ethics, animal housing and care, statistical reporting, ... allowing different parties to express their opinions and concerns, a generally revised version of the Directive is not yet available. The most recent developments can be obtained through the EU DG ENV website⁷.

1.4.2. General Product Safety Directive

The aim of the GPSD [EU, 2001b] is to establish a coherent level of consumer protection for all consumer products on the internal market. Thus, it automatically covers many products which are simultaneously regulated by the provisions of the vertical legislations mentioned under 1.4. The legal provisions of Dir. 2001/95/EC are, however, intended to be fully complementary while conveniently taking up consumer products falling outside the scope of other community legislation (e.g. lighters) [DG SANCO, 2003].

Out of the numerous provisions of the GPSD, the following ones deserve special attention due to their relevance to the cosmetic field [DG SANCO, 2003]:

- The basic principle of the GPSD is that only ‘safe’ consumer products are allowed to be placed on the European market [Art. 3(1)]. A ‘safe’ product is defined as ‘any product which, under normal or reasonably foreseeable conditions of use including duration and, where applicable, putting into service, installation and maintenance requirements, does not present any risk or only the minimum risks compatible with the product’s use, considered to be acceptable and consistent with a high level of protection for the safety and health of persons’ [Art. 2(B); EU, 2001b].

At first sight this completely corresponds with the provision of the Cosmetic Products Directive that a cosmetic product must not cause damage to human health [EU, 1976b]. Nevertheless, it should be noted that the GPSD goes further by also covering e.g. mechanical injuries caused by packaging of cosmetic products.

⁷ http://ec.europa.eu/environment/chemicals/lab_animals/revision_en.htm (consulted November 2007).

- The GPSD describes active post-marketing activities for producers as well as competent authorities. The producers are obliged to perform sample testing, to keep a register of complaints and to inform their distributors. They also need to alert the competent authorities. The latter are expected to take the appropriate steps to coordinate market surveillance and to report every consumer product health risk into the harmonised European RAPEX system. This allows other Member States to take necessary precautions with regard to similar products. The Cosmetic Products Directive includes a market follow-up requirement as part of the information that should be kept readily available to the Member States' competent authorities, but does not include any mandatory filing.
- The GPSD gives the Member States the authority to withdraw products from the market in case they are found unsafe. This provision is not taken up in the Cosmetic Products Directive, which means that for a withdrawal of a cosmetic product from the EU market, reference will be made to the GPSD.

1.4.3. EU Legislation on Prepackaged Products and Nominal Quantities

The term *prepackaged product* covers a wide range of consumer products, among which a large variety of foodstuffs, but also cosmetic products. As early as 1976, Dir. 76/211/EEC related to metrological requirements for prepackaged products introduced the concept of mentioning the EU-harmonised e-sign on the product label in case the metrological requirements specified in the Directive were respected (prepackages between 5 g and 10 kg) [EU, 1976a].

For example, the tolerated error between the actual content (measured weight/volume of product) and the nominal quantity (quantity indicated on the prepackage, i.e. the weight/volume the prepackage is deemed to contain) is not allowed to be exceeded, the nominal quantity needs to be preceded by the e-sign and displayed in correct metrological units and marked in figures of pre-defined sizes depending on the overall size of the package. It must be mentioned that this Directive is currently under revision⁸.

In addition to the above-mentioned metrological requirements related to the use of the e-sign, Dir. 80/232/EEC imposes restrictions on the allowed nominal quantities for skin care and oral hygiene products, hair care and bathing products, alcohol-based cosmetics, deodorants and personal hygiene products and talcum powders [EU, 1980]. However, this was considered to hamper the freedom of producers to provide goods according to consumer tastes and to hinder competition as regards quality and price on the internal market, wherefore Dir. 80/323/EEC is repealed.

⁸ http://ec.europa.eu/enterprise/prepack/metrol_requir/inmetrolog_requir_en.htm (consulted November 2007).

From 11 April 2009 onwards, Member States may not, on grounds relating to the nominal quantities of the package, refuse, prohibit or restrict the placing on the market of prepackaged cosmetics [EU, 2007a].

1.4.4. EU Legislation on Aerosol Dispensers

In 1975, the Council of Europe drafted a Directive dealing with measures for the specific category of aerosol dispensers, independent of their content. The rationale was that, viewing the presence of a gas compressed, liquefied or dissolved under pressure, aerosol dispensers call for specific investigations. Capacities and volumes of individual powder, liquid or gas phases, flammability issues, coating of containers and valve sealing are examples of aspects that need to be addressed before the European ∞ -sign is allowed to be placed on the aerosol dispenser's label [EU, 1975]. Directive 75/324/EEC [EU, 1975] also covers deodorants and any other cosmetic spray.

However, it must be mentioned that this Directive is optional, meaning that Member States can, under their national law, allow the marketing of aerosol dispensers not complying to Dir. 75/324/EEC, provided they do not bear the ∞ -sign [DG ENTR, 2005].

In summary, it can be stated that the above-mentioned horizontal legislations may have an impact on the marketing of cosmetic products in the EU.

It is in particular worthwhile to follow up the usefulness and the evolution of the RAPEX system of the GPSD, since this may be of help to develop the so-called 'cosmetovigilance' approach, a harmonized market surveillance system for cosmetic products. The request for this approach was published at the end of 2006, in a resolution from the Council of Europe, recommending that every European Member State should implement in its national policies a cosmetovigilance system with involvement of all stakeholders (health professionals, consumers and manufacturers). The resolution was inter alia based upon pilot studies conducted in France, Austria and Norway. It provides clear definitions for 'undesirable effects' and 'serious undesirable effects', gives details on how to report these, and specifies the roles of the different stakeholders in the cosmetovigilance procedure. In addition, the need for an information exchange system between governments about serious undesirable effects caused by cosmetic products, is emphasized and leads to the official introduction of the INCOS, which is the cosmetic counterpart of RAPEX [EU, 2006b]. Mainly for the further elaboration of INCOS, which for the moment still is at an informal stage, experience with RAPEX can be of help. Although cosmetovigilance is another challenging aspect of the safety of cosmetics, this book focuses on the safety assessment process of cosmetics as such and therefore does not include detailed schemes of existing and potential innovative post-marketing surveillance procedures.

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