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EEC Cosmetic Directive and Legislation in Europe

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THE LAWS OF THE MEMBER STATES RELATING TO COSMETIC PRODUCTS AND THE 6TH AMENDMENT

The Council of the European Communities in regard to the Treaty establishing the European Economic Community (today, the European Union [EU]) and in particular Article 100 thereof has decided to harmonize legislation in the EU [1,2]. The Directive gives a clear definition of cosmetic products: ''Any substance or preparation intended to be placed in contact with the various external parts of the human body or with the teeth and and the mucous membranes of the oral cavity, with a view exclusively or mainly to clean them, perfuming them, changing their appearance and—or correcting body odours and—or protecting them or keeping them in good condition.'' The philosophy of the Directive is that all products should have equal and immediate access to the market throughout the EU provided that they are proven safe for human use. The Directive has been adapted and modified 29 times between 1976 and 1998. The 6th Amendment has made mandatory by January 1, 1997 that cosmetic products may be marketed only if the labeling bears specific information in legible and visible lettering (Article 6) as follows: the name and address or registered office of the manufacturer or the responsible person for marketing in the Union, the nominal content at the time of packaging, the date of minimum durability and the conditions of storage if appropriate, the conditions of use and warnings, the batch number, the function, the list of ingredients in descending order of weight. Article 7a requires that for control purposes the following information be readily accessible to the competent authorities of the Member State: the qualitative and quantitative composition of the product (perfumes may be coded) (good laboratory procedures [GLP], O.J. EU n° L 15, 17—01—87, p. 29), the physicochemical and microbiological specifications of the raw materials and the finished product, the purity and the microbiological control criteria of the cosmetic product, the method of manufacture (good manufacturing procedures, GMP), the person responsible for the manufacturing or first importation into the EU shall possess an appropriate level of qualification, the assessment of the safety (GLP, Council Directive 87—18—EEC of 18 December 1986), the name and address of the responsible person (who must hold a diploma according to Article 1 of Council Directive 89—48—EEC), undesirable effects if existing, and proof of effect by the nature of effect. The

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competent authority of the Member State shall be notified of the place of manufacture or initial import into the EU of the cosmetic products before the latter are placed on the market, the Poison Information Center shall be informed about the formula, and The European Cosmetic, Toiletry and Perfumery Association (COLIPA) [3] has negotiated that only major deviations from basic formulas shall be indicated (the basic formulas having been given by COLIPA).

The Committee on the Adaptation to Technical Progress of the Directives on the Removal of Technical Barriers to Trade in Cosmetic Products in set up. This Committee is located in Brussels at the European Commission (DG Enterprise, Industry, 200 rue de la Loi, B-1029 Brussels, Belgium, tel; 32 2 299 1111). Article 12 deals with product, that although complying with the Directive, may represent a risk to human health.

The Directive includes seven annexes, and the eighth is pending.

Annex I. Illustrative list by category of cosmetic products.

Annex II. List of substances that must not form part of the composition of cosmetic products. 420 substances are listed. On a time-to-time basis, new substances are included in the list. The cosmetics on the market, containing a newly forbidden substance or an authorized substance revised for a lower concentration, are regulated in the sense that they are ''authorized for a short defined period of time, the manufacturing of the cosmetic in question becoming often forbidden.'' Hormones, anesthetics, chloroform, drug type molecules, and, recently, crude and refined coal tar fall in this category.

Annex III. List of substances that cosmetic products must not contain, except subject to restrictions and conditions. For instance: hydrogen peroxide containing or releasing cosmetics for haircare 12% H_2O_2 is authorized, but for oral hygiene concentration 0.1% only is authorized, and fluorides for oral hygiene products are limited to concentration 0.15% as F.

Annex IV. List of coloring agents allowed for use in cosmetic products. Four classes are given: (1) all purposes, (2) not for use around the eye, (3) exclusively for products not in contact with mucous membranes, (4) and products briefly in contact with the skin.

Annex V. List of substances excluded from the scope of the Directive.

Annex VI. List of preservatives that cosmetic products may contain. For instance, Hexetidine 0.1% as preservative for the product but may be present at higher concentration (justify) as deodorant in soap or antidandruff shampoos.

Annex VII. List of UV filters that cosmetic products may contain.

Annex VIII. A proposal for a pictogram calling the attention of the customer to the information for use.

In summary, the Directive covers every cosmetic (see definition) imported or manufactured within the EU. Cosmetics not allowed for children for safety reasons must carry the warning ''not for children'' or ''not below some year of age.'' Samples and testers are handled under the same Directive. National language for the labels is often required, and ingredients may be given in INCI (International Nomenclature for Cosmetic Ingredients). Manufacturing date is not required, expiration date is required for less than 30 months shelflife. In case of damage and in order to deal with emergency situations, a channel of information is built between the Member States through the ''Poison Information Centers'' or some other national medical instances. Cosmetics are controlled regularly on a random basis, by the Competent Authorities either at the manufacturing site in the EU or at the

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distribution centers, or at the selling points. The methodology for adding new cosmetic ingredients to the existing positive list or modifying the restrictions is as follows: prepare a full dossier from the analytical and safety point of view and submit it to COLIPA [3]. After evaluation, the dossier is sent by the COLIPA ad hoc working party, to the European Commission. At the Commission level the dossier is discussed in the scientific advisory body, the Committee for Cosmetics, and will be published as an amendment in the O.J. EU.

The application may be submitted directly by the applicant to the DG Enterprise, Cosmetic Division in Brussels. The animal testing ban on cosmetic ingredients and combinations is postponed until December 1, 2002. In November 1995, COLIPA [4,5] published two important documents related to the safety information and provision for cosmetics and raw materials in order to prepare the dossiers required by the 6th Amendment. For the provision of safety information for finished products, a process is recommended to be followed by the safety assessor in arriving at the safety assessment. First, a toxicological profile of ingredients must be identified, and second for finished products. For finished products the assessment may take into consideration formulas that can be compared by composition, and a general statement including several products is acceptable.

The information for raw materials is often required at the supplier level. One expects the supplier to consolidate, identity, safety data sheet, toxicology, and human experience (if available). The chairman of the Scientific Committee on Cosmetology of the Commission of the EU, Pr. Loprieno, published in 1992 the views of the Committee [6]. Categories of cosmetic products and exposure levels in use, physicochemical specifications, safety studies in vitro and in vivo, and observation on human subjects are examined in his article, together with toxicokinetics and long-term studies.

The microbiological information on raw materials and finished products is an important part of the dossier [7]. The microbiological quality is identified, by validated methods, for quantitative limits of microorganisms to be 10^3 g or mL and 10^2 g or mL for eye products, baby care, and intimate hygiene, and for qualitative limits the absence of *Pseudomonas aeruginosa*, other gram-negative organisms (enterobacteria), and *Staphylococcus aureus* (*Candida albicans*?).

IMPLEMENTATION OF THE EUROPEAN DIRECTIVE ON COSMETIC PRODUCTS IN THE DIFFERENT MEMBER STATES OF THE EUROPEAN UNION (STATUS JUNE 1998)

The Directive had to be ''normally'' implemented in the 15 Member States within 18 months after the publication in 1993 (6th Amendment). This was not always the case for nationalistic protection and political reasons. The Council of Europe will call the attention of the ''slow'' Member States and even the Justice Court of Luxemburg for nonimplementation. A summary of the situation in the 15 Member States and Norway follows—the data hereafter may have been modified recently, but remains a good way to locate Centers and Authorities.

Austria

After the action of the Commission against the Austrian government, the Directive is now fully implemented, excluding the requirement for licensing and the positive list of active substances. Labelling for ingredients still pending. Qualification: broad definition but re-

lated to qualification in chemistry, food, and drugs. Competent authority: Bundesministerium fur Gesundheit und Konsumentenschutz, Abteilung II—C—16, Radetzkystrasse 2, A-1030 Wien, tel.: 43 1 71172-4668.

Belgium

Implemented since the publication of the Arrêté Royal of October 15, 1997 published in the Moniteur Belge of January 16, 1998. The Belgian Arrêté Royal is for some points more requiring: labelling of ''tested on animals'' must specify for raw materials and/or finished product. Import and manufacturing of products not labelled according to the requirements of Article 5 are authorized until July 1, 1999; after that date only products with a manufacturing date anterior to July 1, 1999 will be accepted. Responsible person qualification as the EEC Directive required. Poison Information Center: Centre Antipoison, rue Joseph Stallaert 1, B-1050 Bruxelles Belgium, tel.: 32 2 345 4545. Competent authority: Ministère des Affaires Sociales, de la Santé Publique et de l'Environment, Inspecteur Mr Féroumont, Inspection Générale des Produits Cosmétiques, Cité Administrative de l'État, Quartier Vésale, B-1010 Bruxelles. Belgium, tel.: 32 2 210 4869.

Denmark

Directive implemented in June 1995. Labelling of all ingredients mandatory since January 1, 1998. Product licencing once a year. Qualification requested according to the Cosmetic Directive. Poison information to: Sundhedsstyrelsen, Fredreikssundsvej 378, DK-2700 Bronshoj, Denmark, tel.: 54 44 889111. Competent Authority: Danish Environmental Protection Agency, Strangade 29, DK-1401 Köbenhaven, Denmark.

Finland

Implementation finalized in the Cosmetic Statute 189—96 and the Decision on Cosmetic Products by the Minister of Trade and Industry 191—96. Fee required for notifications (12 categories and 60 sections). After January 1, 1997 notification before marketing. Poisoning information Center: Central University Hospital in Helsinki. Competent Authority: Finnish Consumer Administration Apnasgatan 4, PB 5 FIN-00531 Helsinki (National Agency: 358 9 473341).

France

As of December 12, 1998 no official implementation of the Directive is known in France; however, the Journal Officiel de la République Français has published until recently several ''décrets'' and ''arrêtés'' on manufacturing sites, preparation of the file, dangerous substances, protection agents, and dyes from 1977 until 1995. These publications make the French Laws (Décret n° 77-1558 du 28 décembre 1977) very close to the Directive, which in practice is applied. The arrêté du 27 janvier 1978 (Journal Officiel- N.C. du 7 février 1978) gives the list of the 16 Poison Information Centers. In Paris, the Centre Antipoisons de Paris is located in the Hospital Fernand Vidal, Madame le Professeur Efthymiou, 200 rue du Faubourg-Saint-Denis, F-75010 Paris, France. Competent Authority: Directions Departementales des Affaires Sanitaires et Sociales (DDASS) via Monsieur Luc Lafay, Ministère de l'Emploi et de la Solidarité, Administration Sanitaire et Sociale, Service de l'Information et de la Communication (SICOM), Bureau de la Communication Interne, 1, Place Fontenoy, F-75007 Paris, France, tel.: 33 1 40 567009.

Germany

The Directive 93-35 EEC has been implemented since December 19, 1996. GMP has been mandatory since June 30, 1997. Information file required since June 30, 1998. Last date for products not in accordance on the market is June 30, 1999. Import notification is required since June 30, 1997. Confidentiality for specific ingredients is authorized (perfumes-coded). For colored cosmetics (makeup, etc.) testing on animals is forbidden. Qualification for responsible person includes chemistry, medical, and pharmaceutical sciences, and many others. The Poison Information Center is: IKW, Karistrasse 21, Frankfurt am Main, D-60329, tel.: 49 692556 1323. Competent Authority: BgW, z. Hd Hern Prof. Dr. Heinemeyer, Tielallee 8892, Berlin, D-14195.

Greece

Directive implemented since April 21, 1997. Notification before the marketing of imported products if Greece is the first Member State. Labelling in Greek language is required in case of difficulty to understand foreign language. Poison Information Center address, via the competent authority: National Drug Organisation (EOF), 284 Mesogion avenue, GR-15562 Holargos, Greece, tel.: 301 654 1964.

Ireland

Directive implemented March 1, 1997 for new products and January 1, 1998 for other products. Notification of manufacturing site or first importation. Qualification as requested by the Directive. Competent Authority: Irish Department of Health, The Earlsfort Center, Earlsfort Terrace, IRL-Dublin 2, Ireland, tel.: 353 1676 8490. Poison Information Center not yet identified.

Italy

Implementation of the Directive: May 16, 1997. June 1998 was the latest date for sale of products not in conformation with the Directive. Ethanol must be labelled for Italian products only. Poison Information Center location to be obtained from the competent authority: Ministero di Sanita, Istituto Superiore di Sanita, Via Regina Helena, 299, I-00161 Roma, Italia, tel.: 39 6 493 87114.

Luxemburg

Directive implemented August 3, 1994. Poison Information Center via competent authority: Ministère de la Santé, rue Auguste Lumière 1, L-2546 Luxembourg, tel.: 352 491191.

Netherlands

Directive implemented October 3, 1995. Poison Information Center via competent authority: Inspectie Gezondheidbescherming, Keuringdienst van Waren, Postbus 777, NL-7500 AT Entschede, tel.: 31 53471111.

Portugal

Directive implemented early 1998, Poison Information Center via competent authority: Instituto da Farmacia e do Medicamento, Parque de Saude de Lisboa, av. do Brazil 53, P-1700 Lisboa, Portugal, tel.: 351 1 790 8500.

Spain

The Directive is implemented since the end of 1998 into a Royal Decrete. Notification to be made at the level of the ''provinces'' who in turn mails a copy to the Dirección General de Farmacia y Productos Sanitarios (DGFPS). Labelling must be understandable to Spanish consumers. Qualification of the responsible person: university degree or equivalent. The information related to poisoning are to be given in urgency to the DGFPS who informs the National Institute for Toxicology (Mahadagonda). Competent Authority: Ministerio de Sanidad y Consumo, Dirección General de Farmacia y Productos Sanitarios, Paseo del Prado 18-20, E-28014 Madrid, Espana, tel.: 34 1 596 4070 (fax preferred for language problems: 34 1 596 1547).

Sweden

Directive implemented since November 4, 1995. Fees 200 Swk per product, maximum 415000 Swk per Company. Poison Information Center: Giftinformationcentrale, Karolinska Sjukuset, Box 60500, S-10401 Stockholm 80, Sweden. Competent Authority: Makamedelsverket (Medical Products Agency) Box 26, Husargatan 8, S-75103, Uppsala, tel.: 46 18174687.

United Kingdom

Directive implemented June 1996, nonconform products accepted until January 1, 1999. Notification for manufacturing site and importation per categories: perfumes, decorative cosmetics, skincare, haircare, and toiletries. Animal testing forbidden from 1998, but the delay will be regulated soon. Qualification: Safety certificates must be signed by pharmacist or a physician holding a United Kingdom diploma. Poison Information Center via competent authorities: Consumer Safety Unit, Department of Trade and Industry, 1, Victoria street London SW1H OET, fax preferred: 44 171 215 0357.

Norway

Not a Member State. Directive implemented in October 1995.

Other European Countries

The Directive 78-768 and the 6th Amendment are applied, sometimes more restrictive in the forbidden molecules. The applicant for importation or local manufacturing is ''recommended'' to follow the Directive. A hearing with the competent authority, the Ministry of Health, is hardly recommended.

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Regulatory Requirements for the Marketing of Cosmetics in the United States

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SCOPE

This chapter discusses the Federal regulatory requirements for the marketing of cosmetics in the United States, under the laws administered by the U.S. Food and Drug Administration (FDA). Federal control of cosmetics is a complex and shared responsibility, and, although this chapter focuses on the FDA's regulation of cosmetic products and their labeling, it also must take note of the overlapping jurisdictions of its sister agencies, the U.S. Federal Trade Commission (FTC), the U.S. Consumer Product Safety Commission (CPSC), and the U.S. Environmental Protection Agency (EPA). It is clearly beyond the scope of this writing to discuss the role played by the State Legislatures and by the State Attorneys-General, but such discussions are readily available to the interested reader elsewhere (1). The role of ''self-regulation'' in the joint oversight responsibility for cosmetics by the FDA and its stakeholders in the industry is also discussed. Finally, the chapter concludes with a brief mention of international harmonization and its impact on cosmetic regulation in the United States.

BASIC U.S. LEGAL STRUCTURE FOR COSMETICS

The FDA is the principal regulatory agency charged with the enforcement of the *Laws* governing the marketing of cosmetics in the United States. The *Laws* are the basic enabling authority enacted by Congress. For cosmetics, the agency is given the mandate for enforcing the statutory requirements of the 1938 Federal Food and Drug and Cosmetic Act (FD&C Act, also referred to as the ''Act''), the 1960 Color Additive Amendments to the Act, and the 1966 Federal Fair Packaging and Labeling Act (FPLA). Under the authority of these statutes, the FDA has promulgated *Regulations* (or *Rules*) to implement the mandate conferred by the *Laws. Guidance Documents*, which include *Policy Statements* (and those documents formerly termed *Advisory Opinions*) have also been issued by the agency. Although not legally binding on the public or on the agency, *Guidance Documents* none-

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theless serve to provide the FDA's interpretation of the *Laws* and applicable *Regulations* (see Figure 1).

Federal regulations of cosmetics involves oversight of print, radio, television, and multimedia advertising as well as of product package labeling. The jurisdiction of the FTC to regulate the advertising of cosmetic and ''Over-the-Counter'' (OTC) Cosmetic-Drug products overlaps that of the FDA, and is largely based upon the portion of Section 5 of the 1914 Federal Trade Commission Act (FTCA) and subsequent amendments and legislation to the FTCA that prohibits ''unfair'' and ''deceptive'' acts or practices (2). the FDA and FTC have established a memorandum of understanding (MOU) to clarify the parameters and boundaries of this relationship (3).

FDA also shares its regulatory responsibilities for the regulation of cosmetics and topical personal care products with other Federal agencies. The U.S. Consumer Product Safety Commission (CPSC) exercises regulatory authority over ''soap'' products not making cosmetic or drug performance claims under the 1960 Federal Hazardous Substances Act (FHSA) and the Consumer Product Safety Act (CPSA) (4e-g); more about the regulation of soap will be discussed later in this chapter. The CPSC also is delegated the authority under the 1970 Poison Prevention Packaging Act (PPPA) for promulgating ''child-resistant'' packaging (CR Packaging) regulations for cosmetic products and soap products (4a); these regulations are codified at *16 CFR 1700.* In recent years, final rules have been promulgated, requiring CR packaging for nail care products (for example, primers) containing ≥5% methacrylic acid (4b), household (artificial nail) glue removers containing acetonitrile (4d), and home cold wave permanent neutralizers containing sodium bromate or potassium bromate (4d). A proposed rule has also been published in the *Federal Register*, which would require CR packaging for fluid cosmetic products (among other categories of household substances) formulated with ≥10% of low viscosity hydrocarbons (≤100 SUS @ 100 deg. F) (4c). Finally, the Environmental Protection Agency (EPA) has regulatory authority over some multi-functional personal care products, such as cosmetic liquids, lotions, or sprays that are also insect repellants. EPA's authority to

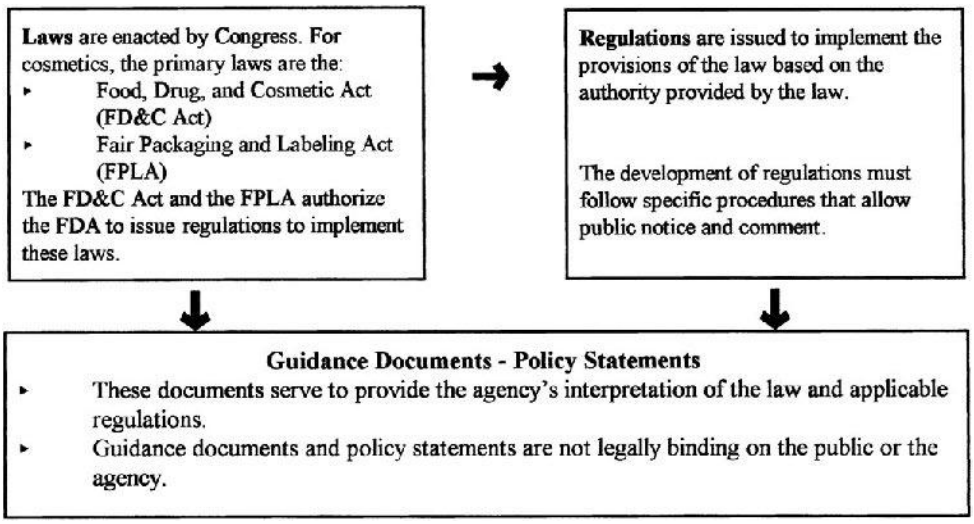


FIGURE 1 Basic U.S. legal and regulatory structure for cosmetics.

regulate such products is derived from the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (5).

Table 1 summarizes the federal agency interrelationships involved in the regulation of cosmetics in the United States.

BASIC U.S. REGULATORY STRUCTURE FOR COSMETICS

Definitions: Cosmetics, Soaps, and Drugs

The statutory definition of ''cosmetic'' is given at Section 201 (i) of the FD&C Act as:

> (1) Articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and (2) articles intended for use as a component of any such articles, except that such term shall not include soap.

For reasons discussed earlier in this book (see Chap. 2), the use of the term ''cosmetics'' refers not only to finished cosmetic products marketed to consumers, but also to constituent ingredients and other components of such finished products (for example, packaging). Under current legal standards, topical products functioning as cosmetics may cleanse, beautify, promote attractiveness, or alter appearance of the human body. The FDA Voluntary Cosmetic Registration Program (VCRP) currently lists 13 subdivided cosmetic product categories, which appear in the codified regulations at *21 CFR 720.4* (see Chap. 2, Table 1).

TABLE 1 U.S. Federal Statutes for Personal Care Products

Cosmetics and OTC drug–cosmetics
Products, ingredients, packaging, and labeling (FDA, CPSC, BATF[a], EPA[b])
Federal Food, Drug, and Cosmetic Act (FD&C Act), 1938
Color Additive Amendments to the FD&C Act, 1960
Federal Fair Packaging and Labeling Act (FPLA), 1966
Federal Hazardous Substances Act (FHSA), 1960
Federal Poisoning Prevention Packaging Act (PPPA), 1970
Federal Insecticide, Rodenticide, and Fungicide Act (FIFRA)[b], 1947
Print and media advertising (FTC)
Federal Trade Commission Act (FTCA), 1914
Wheeler-Lea Act, 1938
Magnuson-Moss Warranty-Federal Trade Commission Improvement Act, 1975
Soap Products
Soap (saponification), FHSA, CPSA
Soap (detergent, ''syndet''[c]), FD&C Act
Soap (combination saponification + ''syndet''), FD&C Act
Soap (with active drug ingredient), FD&C Act
Soap (saponification or ''syndet'' making cosmetic claims), FD&C Act, FPLA

[a] BATF = Bureau of Alcohol, Tobacco, and Firearms (U.S. Dept. of the Treasury), for Specially Denatured Alcohol formulations (see *27 CFR 21*).

[b] Containing pesticide or claiming insect-repellant efficacy.

[c] ''Syndet'' = synthetic detergent.

''Soap'' products are generally exempt from the cosmetic provisions of the FD&C Act, and, indeed, from the definition of ''cosmetic'' given in the statute. The FDA interprets the term ''soap'' at *21 CFR 701.20* to apply to products

> Intended for cleansing the human body
> Labeled, sold, and represented solely as soap
> Consisting primarily of alkali metal salts of free fatty acids (i.e., the bulk of its nonvolatile matter that serves as the detergent)
> Detergent properties of which articles are due to the alkali metal salts of free fatty acids

Liquid and solid product formulations consisting of synthetic detergents (''syndets''), combinations of soap and synthetic detergents (''combo'' bars) intended not only for cleansing but also claiming other cosmetic product performance attributes (e.g., ''beauty bars'' or ''body bars'' claiming to beautify, moisturize, soften, or smooth the skin) must comply with the regulatory requirements applicable to cosmetics (e.g., bear ingredient declarations required at *21 CFR 701.3*). Indeed, even if such detergent or combination soap–detergent products are intended solely for cleansing of the human body, possess the characteristics consumers generally ascribe to ''soap,'' and are identified in labeling as ''soap'' or some fanciful adaptation of this descriptor (e.g., ''sope,'' ''jabon,'' ''liquid soap,'' etc.), these products are still regulated as cosmetics.

The statutory definition of the term ''drug'' is given at Section 201 (g)(1) of the FD&C Act, in pertinent part, as:

> (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention in man . . . and (C) articles (other than food) intended to affect the structure or any function of the body of man . . . and (D) articles intended for use as a component of any [such] articles.

Regardless of their respective legal standings as ''cosmetics'' regulated under the FD&C Act or ''soaps'' regulated under the CPSA/FHSA, personal-care products that are also intended to treat or prevent disease or otherwise affect the structure or functions of the human body are considered ''drugs'' and must comply with these provisions of the law as well as any other provisions as cosmetics or soaps, respectively. Most currently marketed cosmetics that are also drugs are OTC drugs (e.g., 'fluoride' anticaries toothpastes, antiperspirant deodorants, antidandruff shampoos, and sunscreen lotions). However, several drug–cosmetics are ''new drugs'' [6], for which safety and effectiveness had to be proven to the agency before they could be marketed. Analogously, soap products formulated to contain ''active ingredients,'' if intended to cure, treat, or prevent disease, or if intended to affect the structure or any function of the human body, may also be regulated as drugs. This would include, for example ''medicated'' anti-acne soaps, the ''antibacterial'' bar and liquid soaps first introduced into the market in the late 1980s [7], and the alcohol-based liquid ''hand sanitizers'' of the late 1990s [8].

Statutory Controls on Cosmetics

The FD&C Act not only defines the term ''cosmetic,'' but sets forth the basic requirement that cosmetic products introduced into interstate commerce within the United States must be safe for their intended use and properly labeled. The act accomplishes this by explicitly prohibiting the adulteration or misbranding of cosmetics, and the introduction into, or

receipt in, interstate commerce of ''adulterated'' or ''misbranded'' cosmetics (see FD&C Act, Sections 601 and 602, respectively).

Adulterated Cosmetics

A cosmetic is ''adulterated'' according to the FD&C Act, Section 601 (a)–(e) if:

- It bears or contains any poisonous or deleterious substance, which may render it injurious to users under the conditions of use prescribed in the labeling or under ''customary or usual'' uses
- It consists wholly or in part of any filthy, putrid, or decomposed substance
- It has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health
- Its container is composed, wholly or in part, of any poisonous or deleterious substance that may render the contents injurious to health
- It is not a hair dye and it is, or bears or contains, a color additive that is unsafe within the meaning of the act

Coal-Tar Hair-Dye Exemption. The FD&C Act exempts so-called ''coal-tar'' hair-dyes from the adulteration provision at Section 601 (a), if they bear the cautionary statement prescribed by law on the label and give ''patch test'' instructions, even if they are irritating to the skin or are otherwise harmful to the human body. The ''coal-tar hair-dye exemption,'' named for the synthetic organic colors originally derived from the coal tar derivative, aniline, to which the exemption was initially applied [9], does not include eyelash and eyebrow dyes since coal-tar derived color additives may cause blindness when used for dyeing the eyelashes or eyebrows (9c). The exemption also does not apply to non-coal tar color additives in hair dyes (9c).

Sources of Adulteration. Cosmetic adulteration may be associated with unintentional trace level contaminants (e.g., *N*-nitrosamines, or 1,4-Dioxane) of the ingredients (also referred to as 'raw materials') employed in finished cosmetic products [10–12] or to the manner of product formulation. Quality control problems (e.g., pH) or failure to follow good manufacturing practices guidelines [13] can also result in deviations of particular product batches from master formula specifications. In the past four (4) fiscal years (FY96–FY99), the FDA has found that approximately 88% of cosmetic product adulterations subject to voluntary recall actions (see ''Recalls'' in Law Enforcement of FD&C Act Violations, below) were most frequently related to problems of microbiological contamination (see Table 2) [14].

TABLE 2 Cosmetic Product Voluntary Recalls

	FY 1996	FY 1997	FY 1998	FY 1999
Total recalls	26	9	9	9
Microbiology recalls	23	8	8[a]	8
Misbranding recalls	3	1	0	1
Other recalls	0	0	1[b]	0

FY = fiscal year.
[a] 6 Class II Microbiology + 2 Mold.
[b] 1 Class II pH.

Misbranded Cosmetics

A cosmetic is ''misbranded'' according to the FD&C Act, Sec. 602 (a)–(f) if:

Its labeling is false or misleading in any particular
Its package label fails to contain the name and place of business of the manufacturer, packer, or distributor, as well as an accurate statement of the quantity of the contents in terms of weight, measure, or numerical count
Any word, statement, or other information required to appear on the label is not prominently and conspicuously placed and in terms likely to be read and understood by the ordinary consumer under customary conditions of purchase and use
Its container is made, formed, or filled in a manner likely to be misleading
It is a color additive, unless its packaging and labeling are in conformity with requirements in the regulations
Its packaging or labeling are in violation of an applicable regulation issued under the 1970 PPPA.

A cosmetic is misbranded as a consumer commodity according to the FPLA, Section 7, if it is introduced or delivered for introduction into commerce in violation of any of the provisions of the law or its implementing regulations, including the requirements contained in Sections 4 and 5 of the FPLA, which provide that the label of a commodity must state:

The identity of the commodity
The name and place of business of the manufacturer, packer, or distributor
The net quantity of contents (in terms of weight, measure, or numerical count) separately and accurately stated in a uniform location upon the principal display panel (PDP)
The ''common or usual name'' of the commodity and, if it contains two or more ingredients, the ''common or usual name'' of each ingredient listed in order of decreasing predominance, with the exception of such ingredients deemed to constitute a ''trade secret.''

Law Enforcement of FD&C Act Violations

Violations of the adulteration and misbranding provisions of the act may subject the violator to various enforcement tools available to the FDA. These include (but are not limited to) (16c):

Warning letters, subject to public disclosure under the Freedom of Information Act (FOIA), may be posted on the Internet FDA Web site and are regularly publicized in the trade press and industry newsletters such as *The Rose Sheet*
Targeted establishment inspections and sampling programs
Seizure of cosmetic goods alleged to be in violation of the FD&C Act (civil actions)
Detention of imported cosmetics offered for entry into U.S. interstate commerce that appear to be in violation of the law (see, for example, FD&C Act, Section 801(a)
Injunction proceedings against firms or individuals, seeking that a company cease present and future manufacture and distribution of cosmetic products until compliance with the law can be assured

Criminal prosecution of responsible persons within violator cosmetic firms

Recalls. Recall and Field Correction are actions taken by a firm to either remove a product from the market or to conduct a field correction. Recalls of cosmetic products, may be conducted on a firm's own initiative or by FDA request. The FDA has no authority under the FD&C Act to order the recall of a defective or possibly harmful cosmetic product, although it can request a firm to recall a product. Resistance to an FDA request for voluntary recall can, however, trigger other enforcement actions by the agency, which have recently been reviewed by Calogero [15]. The FDA has defined policies concerning such voluntary cosmetic (as well as food, drug, and medical device) product recalls; these are codified at *21 CFR 7.45–7.59*, and additional guidance can also be found at the FDA website (*http://www.fda.gov*). The FDA's regulations divide recalls into three categories:

Class I Recall Products that are clearly dangerous or defective that pose clear or irreversible hazards to the public health; there is reasonable probability that the use of or exposure to a violative product will cause serious adverse health consequences or death *(21 CFR 7.3 (m)(1))*

Class II Recall Products that are intermediate in their potential for adverse public health consequences, but may cause a temporary or reversible health problem; use of or exposure to a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote *(21 CFR 7.3 (m)(2))*

Class III Recall Products that are unlikely to cause any adverse health reaction but that violate FDA regulations; use of or exposure to a violative product is not likely to cause adverse health consequences *(21 CFR 7.3 (m)(3)).*

Regulatory Controls on Cosmetics

Cosmetics marketed in the United States, whether manufactured domestically or imported from abroad, must be in compliance with the provisions of the FD&C Act, the FPLA, and the regulations published under the authority of these laws. Yet, cosmetics are arguably the least regulated category of articles subject to the jurisdiction of the FD&C Act [16]. There is no premarket approval requirement for cosmetic products or their constituent ingredients under the law. Other than color additives and those few ingredients restricted or prohibited by regulation from use in cosmetics, no mandatory regulatory controls exist on the chemistry and structure substantiation of the ingredients themselves, conditions of manufacture of the finished cosmetic products, or safety testing that the ingredients and products must undergo prior to marketing; no premarket test results need be submitted to the FDA.

The FDA has therefore promulgated regulations and guidance documents to help ensure that only cosmetics that are safe for their intended use and are neither ''adulterated'' nor ''misbranded'' enter interstate commerce. These regulatory documents address the following issues.

Cosmetic Safety

Cosmetics are not currently subject to the same FDA safety and effectiveness standards as are drugs, biologics, and medical devices. The FD&C Act does not require that cosmetic manufacturers or marketers test their products for safety, nor does the FDA specify particular test batteries or preclinical (i.e., animal or in vitro alternative tests) and human clinical safety tests by cosmetic product category that marketers must use to substantiate cosmetic

product safety. Neither are manufacturers or marketers of cosmetic products required to submit the results of such safety substantiation tests to the agency on a premarket approval basis. Nonetheless, the FDA strongly urges cosmetic manufacturers and/or raw material suppliers to conduct safety substantiation assessments and whatever toxicological or other tests are appropriate to substantiate the safety of their cosmetic products and the ingredients formulated therein prior to marketing them. If the safety of a cosmetic is not ''*adequately substantiated*,'' the product may be considered misbranded and may be subject to regulatory enforcement action unless the label bears the following statement, using the exclusivity language found at *21 CFR 740.10(a)*:

''*Warning*—The safety of this product has not been determined.''

Cosmetic Ingredients

The FD&C Act provides no statutory authority for the premarket approval of cosmetic ingredients. This is reflected in the FDA's regulations, which are generally silent on the subject of permitted or ''positive listed'' cosmetic ingredients. With the sole exception of color additives (see *21 CFR 70-82*), which are subject to premarket approval, and a few ''negative listed'' or prohibited/restricted ingredients at *21 CFR 700* and 21 CFR 250.250 (see Table 3), a cosmetic manufacturer may use virtually any raw material as a cosmetic ingredient (regardless of whether it was specifically designed for use in cosmetic end-use applications) and market the finished cosmetic product without premarket approval [18]. Of course, the marketer of the finished cosmetic product bears legal responsibility for any adverse reactions experienced by consumers or public health consequences that may result from this action. The number of ingredients used in cosmetics has grown exponentially since the early 1970s. For example, the *Eighth (8th) Edition* of the *CTFA*

TABLE 3 Cosmetic Ingredients Prohibited or Restricted in the United States[a]

By regulation (*21 CFR 700*, *21 CFR 250.250*)
Bithionol
Mercury compounds
Vinyl chloride
Halogenated salicylanilides
Zirconium complexes (aerosol cosmetics)
Chloroform
Methylene chloride
Chlorofluorocarbon propellants
Hexachlorophene[b]
Miscellaneous ingredients of regulatory concern[a]
100% Liquid methyl methacrylate monomer (in nail products)[c]
≥5% Formaldehyde (in nail products)
Acetylmethyltetramethyltetralin (AETT) (in fragrances)
Musk ambrette (MA) (in fragrances)
6-Methylcoumarin (6-MC) (in fragrances)

[a] See *FDA's Cosmetics Handbook*, 1994 Edition, p. 8.
[b] *21 CFR 250.250.*
[c] *Source*: A.R. Halper to J. Nordstrom (President, Nail Manufacturers Council), personal communication, September 20, 1996.

International Cosmetic Ingredient Dictionary (CID) [19], one of the most authoritative tabulations of cosmetic ingredients, contains monographs for approximately 10,500 such raw materials (see Fig. 2).

Color Additives

The term ''color additive'' is defined in the FD&C Act at Section 201 (t) and by regulation at *21 CFR 70.3 (f)*. Except for ''coal tar hair dyes'' used to color the hair (of the scalp), the 1960 Color Additive Amendments to the FD&C Act require that color additives used in food, drugs, medical devices, and cosmetics be approved by the FDA for their intended use, a process that requires both chemistry and safety reviews of the color additive by color chemistry and toxicology staff experts at the FDA. A cosmetic containing an ''unlisted'' color additive (i.e., a color additive that has not been approved by the FDA for its intended use) is considered adulterated and subject to regulatory action. Color additives listed at *21 CFR 73* (predominantly of inorganic (mineral) or botanical origin) are exempt from the FDA's ''batch certification'' requirements (see *21 CFR 80*). Color additives listed at *21 CFR 74* are largely synthetic organic dyes and pigments (i.e., so-called ''coal tar'' colors) and are subject to the FDA's ''batch certification'' requirements at *21 CFR 80*; provisionally listed color additives, including color additive lakes, are listed at *21 CFR 82*. FDA recently published in the *Federal Register* a proposal to permanently list color additive lakes [20]; proposed simplifications in nomenclature for declaring straight colors and their lakes were also included as part of this proposal. It is important to note that all batches of certifiable color additives must actually be tested, certified in the FDA's laboratories for compliance with the identity and specifications established by regulation for that color additive, and issued a certification number before they may be represented and sold as an FDA-certified color additive.

FDA listing regulations for color additives specify permitted end-use applications, which may be general or specific in nature, sometimes with restrictions in permitted uses

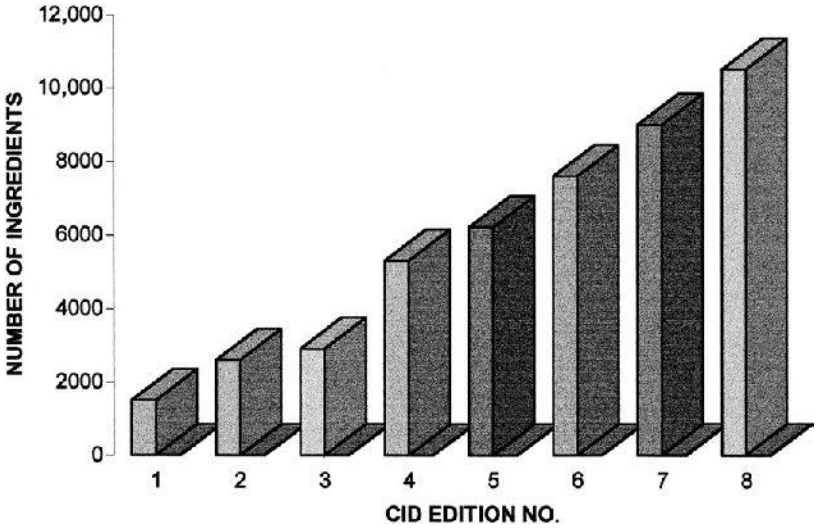


FIGURE 2 Cosmetic ingredient growth. (From J. A. Wenninger and R. C. Canterbery, personal communications.)

or allowed concentrations. Cosmetic color additives, for example, may be listed for general use in imparting color to product formulations, for use in decorative cosmetics intended for external application to the hair and other appendages of the human body (other than the area of the eye), or may be specifically listed, solely or together with other cosmetic product applications, for eye area use [21]. Only color additives specifically authorized by regulation for use in the area of the eye may be legally used for such applications. Only one color additive, dihydroxyacetone (DHA), is specifically listed for an intended use in externally applied cosmetics ''to impart a color to the human body''; this finds widespread application in today's ''sunless'' or ''self-tanning'' cosmetic products [22]. No color additives are currently approved for use in injectable cosmetic tattoos [23]. Further details about the color additives currently listed (approved) by regulation for use in cosmetics in the United States may be found on the Internet at FDA's website (e.g., http://www.cfsan.fda.gov/cosmetics.html).

Cosmetic Labeling

Cosmetic products distributed in the United States must comply with the labeling regulations published by the FDA under the authority of the FD&C Act and the FPLA [24a]. Section 10(a) of the FPLA gives the FDA authority to require labeling of products considered ''consumer commodities''; that is, products regulated under the FD&C Act, which are ''customarily produced or distributed for sale through retail sales . . . for consumption by individuals, or use by individuals for purposes of personal care or in the performance of services ordinarily rendered within the household'' [24b].

The statute requires that products be honestly and informatively labeled so that consumers can conduct ''value comparisons'' at the point of purchase; that is, in order to determine what ingredients are in a product and which product among several alternatives being considered for purchase is the best value. This determination includes medical considerations, since the FDA has previously concluded [25] that a cosmetic product or ingredient to which a consumer is allergic (and which the consumer therefore cannot use) has no value to such a consumer.

''Labeling'' refers to actual product package labels as well as other written, printed, or graphic material on or accompanying a product (e.g., hangtags, promotional fliers, package inserts). Label statements required under the FD&C Act must appear on both the inside as well as the outside container or wrapper, if any; FPLA requirements need only appear on the label of the outer container or wrapper.

Cosmetic product package labeling regulations enacted under authority of the FD&C Act and/or the FPLA require that cosmetic labels bear certain fields of information that provide the consumer with proper identification and other data that will enhance the consumer's understanding of the product being purchased and facilitate the ability of the consumer to contact the manufacturer or distributor of the product, should there be a need to do so. Although the cosmetic labeling regulations at *21 CFR 701* generally require all labeling information to be written in the English language commonly understood by most American consumers, *21 CFR 701.2 (b)* also provides certain accommodations in the case of articles distributed in Puerto Rico or other territories in which the predominant language is other than English. The required fields of information include the following:

Statement of identity (i.e., common name) rendered in bold type on the cosmetic product principal display panel; note that this is an FPLA requirement for cosmetics, not an FD&C Act requirement per se

Name and address of manufacturer (or packer or distributor)

Net quantity of contents (net weight or count or measure, as customary or as required). English units are mandatory in the United States but a technical amendment to the FPLA under the 1991 American Technology Preeminence Act (ATPA), as revised in 1992 [26a,b], and more recent regulatory proposals to implement the ATPA provisions for FDA-regulated products [26c], now advocate the use of the most appropriate units of the metric international system (SI) of weights or measures, wherever practicable. This proposal includes the dual declaration of net quantity of contents in terms of both English units and the international metric (SI) system of weights or measures

Cosmetic ingredient label declarations (see below)

Warning statements (or cautionary statements) concerning safe use, as required at *21 CFR 740* (see below)

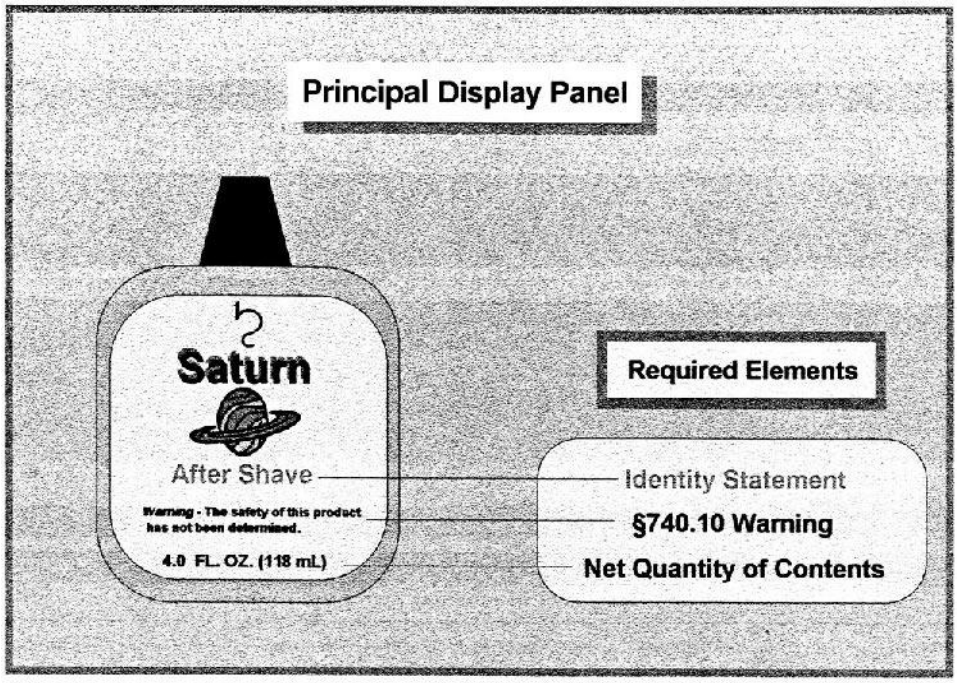
A typical cosmetic product package label exemplifying these features is shown in Figure 3.

Cosmetic Ingredient Label Declarations

Section 5(c)(3) of the FPLA specifically authorizes FDA to promulgate regulations requiring the declaration of all cosmetic ingredients on product package labels of cosmetics considered ''consumer commodities'' (*loc. cit.*, Ref. 24(b)); these regulations are codified at *21 CFR 701.3*. Exempt from the ingredient declaration requirement are professional cosmetic products, such as hair and skin preparations or makeup products used by cosmetologists, beauticians, or aestheticians on clients at professional establishments such as salons, spas, and theaters, provided that these products are not also sold to consumers through the professional establishments, workplaces, or other miscellaneous beauty supply retail outlets for their consumption at home; such cosmetics are not legally considered ''consumer commodities.'' Similar exemptions apply to ''free'' (gratis) samples, gifts, cosmetics distributed as free amenities at hotels, and cosmetics and toiletries made available to workers and visitors (but not sold) for on-site use at occupational settings, such as construction sites, hospitals, clinics, etc. However, cosmetic products offered as ''gift with purchase'' are ''consumer commodities'' and subject to the ingredient declaration requirement, because the ''gift'' is only available in conjunction with a retail sale. Professional cosmetic products exempt from the ingredient declaration requirement are frequently labeled ''for professional use only.''

Ingredient declarations must be ''conspicuous'' and ''prominent'' in placement on any appropriate information panel of the outer container, and not less than certain size specifications in relationship to the size and shape of the product package, in order to ensure that the declaration is likely to be read at the time of purchase by the consumer.

FPLA labeling requirements specify that cosmetic ingredients must be declared, in descending order of predominance (see *21 CFR 701.3 [a]*), utilizing ingredient names derived in hierarchical order of precedence from the nomenclature sources specified by regulation (see *21 CFR 701.3 [c]* and *701.30*); alternatively, the ingredients may be grouped and the groups declared according to *21 CFR 701.3 (f)*. The ''common or usual'' names specified by regulation in the United States are required to be stated in the language understood by American consumers, namely English, except as provided at *21 CFR 701.2 (b)* (see Cosmetic Labeling, p. 746, loc. cit.). Cosmetic ingredients present at one percent or less ($\leq$1%) may be declared after ingredients present at higher levels without regard to order of predominance, and fragrance and flavor, if any, being complex compositions of matter in themselves, may be declared for purposes of product package label-



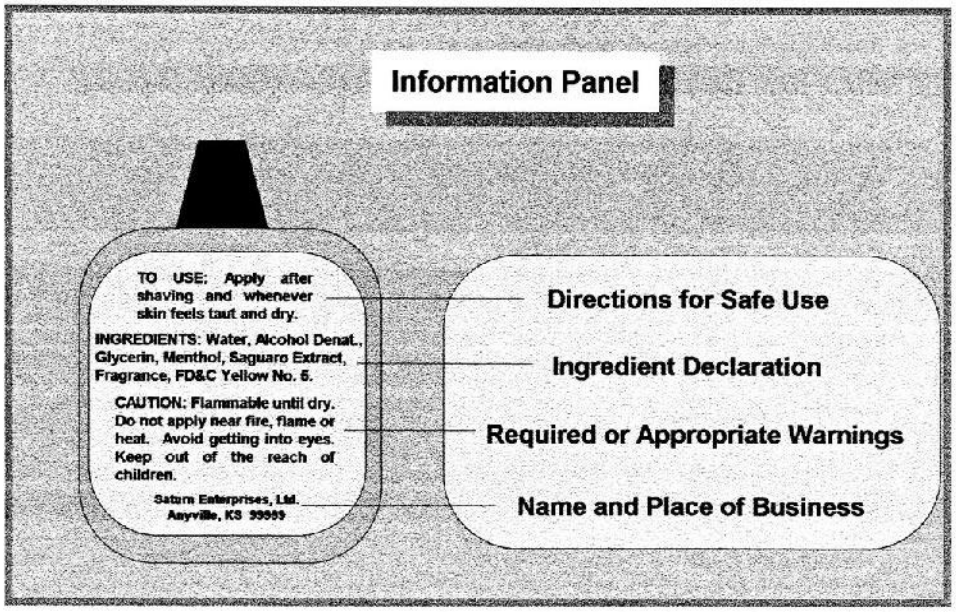


FIGURE 3 Typical cosmetic label elements. (Note: For illustrative purposes only. See *21 CFR 701* for correct letter heights and proportions.)

ing as ''flavor'' and ''fragrance,'' respectively. ''Incidental ingredients'' (see *21 CFR 701.3 [1]*) need not be declared, and those ingredients accepted by the FDA as exempt from public disclosure and granted ''confidentiality'' or ''trade secret'' status may be declared as ''and other ingredients'' (see *21 CFR 720.8*).

''Soap'' products meeting the requirements of *21 CFR 701.20(a)(1)* and *(a)(2)* are exempt from the FPLA requirement for mandatory label ingredient declarations applicable to cosmetics.

The manner of declaration of ingredients in OTC drug–cosmetic products is specified at *21 CFR 701.3(d)*, as recently amended (see 64 FR 13234–13303@13297, March 17, 1999). Drug ''active ingredients'' present in OTC drug–cosmetic product formulations are declared first, as required at *21 CFR 201.66(c)(2)* and *(d)* of this chapter, and following the standard-format ''Drug Facts'' information fields (i.e., ''Use(s),'' ''Warnings,'' ''Directions,'' and ''Other Information''), any ''inactive'' or cosmetic ingredients are declared in descending order of predominance or grouped, in accordance with the provisions of *21 CFR 701.3(a)* and *(f)*, respectively. An exception in the manner of declaration of inactive or cosmetic ingredients is provided for, if there is a difference in the labeling provisions in *21 CFR 201.66* and Sections 701.3 or 720.8; under these circumstances, the labeling provisions at *21 CFR 201.66* are controlling (see *21 CFR 201.66(c)(8)* and *(d)* of this chapter).

Recent efforts to achieve ''international harmonization'' with cosmetic ingredient nomenclature standards required by the 1976 European Union (EU) Cosmetic Directive [27] and its more recent amendments [28] have resulted in the FDA agreeing to exercise regulatory discretion toward the interim use of parenthetical ''dual declarations,'' employing systematic Linne (Latin) taxonomic genus/species nomenclature for certain categories of ingredients (i.e., botanicals and/or ''trivial'' ingredients) pending review of a citizen petition submitted by CTFA [29]. Color additives are named using the monograph titles in their respective listing regulations (see *21 CFR 73, 74, 82*), although, here, too, the impact of ''international harmonization'' efforts has resulted in the FDA agreeing to exercise regulatory discretion towards the interim use of parenthetical ''color index (CI) numbers'' in a dual declaration [29]. Examples of the new interim ''harmonized'' ingredient declarations are given in Table 4.

Cosmetic Label Warnings

Cosmetics that may be hazardous to consumers when misused must bear appropriate label warnings and adequate directions for safe use. Manufacturers and marketers of cosmetics have a general responsibility to ensure that the labels of their finished cosmetic products bear a warning statement whenever necessary or appropriate to prevent a health hazard that may be associated with the product (*21 CFR 740.1[a]*). These warning statements must be prominent and conspicuous (*21 CFR 740.2*). Some cosmetics must also bear more specific label warnings or cautions prescribed by regulation. Specific cosmetic product categories requiring such statements currently include:

Cosmetic products for which adequate substantiation of safety has not been obtained (*21 CFR 740.10*)
Cosmetics in self-pressurized containers (*21 CFR 740.11*)
Feminine deodorant sprays (*21 CFR 740.12*)
Foaming detergent bath products (*21 CFR 740.17*)
''Coal tar'' hair-dyes posing a risk of cancer (*21 CFR 740.18*) [*Effective date stayed at 47 FR 7829, February 23, 1982*.]

TABLE 4 Selected Examples of U.S. Cosmetic Labeling Names, EU Cosmetic Labeling Names, and Proposed Interim Harmonized Cosmetic Labeling Names

U.S. cosmetic ingredient (U.S. INCI labeling name)	EU cosmetic ingredient (EU INCI labeling name)	Proposed interim harmonization (EU/U.S. dual declaration)
Color additives		
FD&C Green No. 3	Cl 42053	Green 3 (Cl 42053)
D&C Orange No. 4	Cl 15510	Orange 4 (Cl 15510)
D&C Blue No. 1 Aluminum Lake	Cl 42090	Blue 1 Lake (Cl 42090)[a]
Ext. D&C Violet No. 2	Cl 60730	Ext. Violet 2 (Cl 60730)
Botanicals		
Peach leaf extract	Prunus persica	Peach (prunus persica) leaf extract
Sambucus nigra extract[b]	Sambucus nigra extract	Sambucus nigra extract
Sweet cherry pit oil	Prunus avium pit oil	Sweet cherry (prunus avium) pit oil
Oat flour	Avena sativa flour	Oat (avena sativa) flour
Denatured alcohols		
SD Alcohol 38B[c]	Alcohol denatured (Alcohol denat.)	Alcohol denatured (Alcohol denat.)
''Trivial'' ingredients		
Water	Aqua	Water (aqua)
Fragrance	Parfum	Fragrance (parfum)
Tallow	Adeps bovis	Tallow (adeps bovis)
Yeast extract	Faex	Yeast (paex) extract
Goat milk	Caprae lac	Goat milk (caprae lac)
Beeswax	Cera alba	Beeswax (cera alba)
Honey	Mel	Honey (mel)
Sea salt	Maris sal	Sea salt (maris sal)
Egg oil	Ovum	Egg (ovum) oil
Silk powder	Serica	Silk (serica) powder
Mineral oil	Paraffinum liquidum	Mineral oil (paraffinum liquidum)
Coal tar	Pix ex carbone	Coal tar (pix ex carbone)
Fish extract	Pisces	Fish (pisces) extract
Pigskin extract	Sus	Pigskin (sus) extract
Mink oil	Mustela	Mink (mustela) oil

[a] Annex IV of the EEC Cosmetic Directive 76/768/EEC provides that, for those color additives allowed for use in cosmetic products, the lakes or salts of these coloring agents using substances not prohibited under Annex II or not excluded under Annex V from the scope of the Directive are equally allowed and may also be declared under the same Color Index Number as for the corresponding straight color additive.

[b] Certain botanical (plant) ingredients may have Linne System (Latin genus/species) names that have no English language 'common or usual name' equivalents.

[c] *27 CFR 21.*

Cosmetic suntanning preparations not containing a sunscreen (*21 CFR 740.19*) [*Effective date: May 22, 2000.*]

Tamper-Resistant Packaging

The FDA is given the authority under Sections 601 (a) and (c) and 701 (a) of the FD&C Act to issue package security requirements for cosmetics. Requirements for tamper-resis-

tant packaging for *cosmetic liquid oral hygiene products* (e.g., mouthwashes and breath fresheners) and all *cosmetic vaginal products* (e.g., douches and tablets) were promulgated at *21 CFR 700.25*. Details about such packaging is found in the FDA's *Cosmetics Handbook* [30] and at the FDA website, *http://www.fda.gov*.

Cosmetic Good Manufacturing Practices Guidelines

The FDA has never published current good manufacturing practice (cGMP) regulations for cosmetics, although the agency has actively promoted good manufacturing practices by firms marketing cosmetics in the United States. The agency has published *Cosmetic Good Manufacturing Practice Guidelines*, patterned in pertinent part after the food cGMP regulations [13a] but applicable to the cosmetic manufacturing environment, in the FDA's Cosmetics Handbook [13b]; the latter document references the *FDA Investigation Operations Manual (IOM)* [31]. The *Cosmetic Good Manufacturing Practice Guidelines* is a guidance document reflecting FDA policy, but it is not legally binding, either on the cosmetics industry or on the agency. The FDA has also published drug cGMP regulations [32], which apply to prescription drugs and cosmetic–drugs (i.e., OTC drug products making cosmetic claims).

The Voluntary Cosmetic Registration Program

The FD&C Act does not require cosmetic firms to register manufacturing establishments or formulations with the FDA, nor does it mandate that companies submit product adverse reaction report data. Nevertheless, the FDA has encouraged the voluntary registration of such data as being in the public interest and consistent with the spirit of responsible ''self-regulation'' advocated by the cosmetic industry. In the early 1970s, the FDA developed a three-part system of regulations, under which manufacturers or distributors of cosmetics may submit this information to the agency on a voluntary basis [33]. The three parts of the *Voluntary Cosmetic Registration Program (VCRP)* originally comprised the following:

Part I *Cosmetic Establishment Registration Program (CERP)*, requests that cosmetic manufacturing sites be registered with the FDA (see *21 CFR 710*)

Part II *Cosmetic Product Ingredient Statements (CPIS)*, requests that cosmetic formulations and cosmetic raw material composition statements be registered with the FDA (see *21 CFR 720*). This regulation also set forth the 13 product category codes (PCC) at *21 CFR 720.4* recognized by the FDA as ''cosmetic'' functions. Semi-quantitative raw material disclosures were abandoned and purged from the VCRP database in the early 1990s [34].

Part III *Product Experience Reports (PER),* discontinued in 1996 (35), requested the annual filing of ''reportable'' adverse reactions (see *21 CFR 700.3 [q]*) to the use of cosmetic products by manufacturers which the FDA (euphemistically called 'product experiences' (see *21 CFR 730*). The use of optional 'screening' protocols to be filed with the FDA, designed by individual manufacturers, for use in determining the 'reportability' of experiences, was also provided for in the PER Program (see *21 CFR 700.3 (p)*, *730.4 (d)(2)*). This data was collected, tabulated, and analyzed for statistical deviations of individual products from industry-wide adverse reaction trends by product category.

Despite its voluntary nature, the VCRP has never enjoyed full industry participation. Table 5 illustrates the VCRP registration statistics for the years 1992–1996, the last five fiscal years during which all parts of the VCRP were in operation. *Part III (PER)* annual filings by firms considered by the FDA to be eligible to participate in the program have

TABLE 5 FDA Voluntary Cosmetic Registration Program (VCRP), FY 1992–FY 1996

	FY 1992	FY 1993	FY 1994	FY 1995	FY 1996
Establishments registered	939	969	954	757	773
Companies filing formulations	800	782	810	806	684
Formulations registered	18,012	18,369	16,929	18,558	15,982
Companies filing product experience reports	114	116	113	97	75

FY, Fiscal Year
Source: J. E. Bailey, Ph.D., personal communication, July 7, 2000.

historically been the lowest of the three parts of the VCRP. *Part III (PER)* was discontinued in 1996 [35] and the VCRP itself was temporarily put into operational abeyance in 1998 due to resource re-allocations within the FDA [36]. With partial funding restoration by the Congress ''earmarked'' specifically for the FDA's Cosmetics Program, Parts I and II of the VCRP were restarted in 1999 [37], and a new, streamlined electronic World Wide Web-based system to facilitate industry participation is being developed at the time of this writing [38].

Self-Regulation

As the cosmetic industry in the United States has grown and matured, the regulatory paradigm for cosmetics in the United States has evolved from a program based on the *1938 FD&C Act* and lacking Federal pre-market approval authority into a leveraged program of industry ''self-regulation,'' with shared roles played by the FDA's other stakeholders, particularly the cosmetic industry trade associations and consumer advocacy groups. Programs that support industry self-regulation have been initiated by both government and private industry; they include:

The *FDA Voluntary Cosmetic Registration Program (VCRP) (loc. cit.)*;

The *Cosmetic Ingredient Review (CIR)*. Originated in the 1970s as a cosmetic industry initiative [39], CIR is a program funded by the CTFA that assesses the safety of cosmetic ingredients, with full albeit *ex-officio* (non-voting) liaison participation by the FDA, industry, and consumer advocate stakeholders. The CIR does not generally assess the safety profiles of ingredients that are reviewed by the FDA as ''active ingredients'' of drugs (OTC or prescription), nor does it conduct safety assessments of fragrance materials;

The *Research Institute for Fragrance Materials (RIFM)* evaluates the safety profiles and publishes monographs concerning fragrance materials, while the *International Fragrance Association (IFRA)*, a trade association of national fragrance trade associations, establishes usage guidelines for fragrance materials by industry fragrance houses [40].

The FDA's VCRP and the industry-sponsored *CIR* and *RIFM/IFRA* programs are important components of the government-industry cooperation that characterize current efforts towards the successful implementation of self-regulation of the cosmetic industry in the U.S. Other elements of self-regulation include:

Federal Statutes. The *Lanham Act (1946)* empowers companies to seek judicial redress in the federal district courts for unfair business practices resulting in negative impact on market share [41]. The *Robinson-Patman Act (1936)* enables companies to seek to recoup lost sales and profits ascribed to anticompetitive, predatory pricing tactics [42].

Advertising Self-Regulation, NAD/CBBB. Disagreements regarding product performance advertising claims are frequently addressed by competitor/peer-review challenges brought through the self-regulatory protocols of the *National Advertising Division (NAD)*, an arm of the *Council of Better Business Bureaus (CBBB)* [43], and its appeals panel, the *National Advertising Review Board (NARB)*. Failure to resolve advertising controversies through these self-regulatory processes can result in an ultimate referral by the NARB to the FTC. Scrutiny of proposed storyboards prior to being accepted for mass-media air-time is also undertaken by advertising agency legal departments and television/radio network standards and practices boards (e.g., network censors) [44]

The cosmetic industry is characterized by highly competitive marketing strategies and depends on the freedom to rapidly introduce new, innovative cosmetic products to the marketplace without lengthy delays. It is hardly surprising, therefore, that the industry has sought to portray itself as responsible enough to self-police its own manufacturing and marketing practices, or that it has argued [45] that existing laws and FDA regulatory programs concerning cosmetics, together with the industry's commitment to self-regulation and product safety, provide ample consumer protection, given the apparent low risk inherent in cosmetics relative to other categories of products regulated by the FDA. Steinberg [46] advocates compliance within a self-regulatory environment as being in the industry's own self-interest. He observes that regulatory compliance can be a ''win-win'' end result for the industry, consumers, and regulators alike, and cautions that trying to ''*beat the system may succeed in the short term, but it results in significant long-term losses*.'' Steinberg notes that lost sales, public reputation, and market share are the obvious short-term consequences likely to be suffered by noncompliant firms. Widespread noncompliance can also place the current self-regulatory system itself at risk.

International Harmonization and Future Regulatory Challenges

The U.S. regulatory scheme for cosmetics is based on the axiom that cosmetics marketed in the U.S. are safe for their intended use and unlikely to present a major public health risk [47], which is reflected in the lack of pre-market approval authority for cosmetics included in the original 1938 FD&C Act.

Although many of the regulatory systems of other countries have similar goals to those of the United States, such as protecting public health and safety and promoting trade [48], the means by which these goals are achieved may be quite different from the U.S. system. These differences are often based upon the culture of the particular country and can influence not only specific regulatory requirements, such as labeling, but also the fundamental definition of what constitutes a cosmetic. Several categories of topical prod-

ucts regulated as OTC drugs or OTC drug–cosmetics in the United States, such as sunscreens, skin bleaches, antiperspirants, and antidandruff shampoos [49], are regulated as cosmetics under the EU Cosmetics Directive of 1976 [27]. Japan, which currently regulates cosmetics according to a system of premarket approval and licensure rather than the postmarket surveillance system used by the United States or the notification system used by the EU, allows cosmetics to have some effect on the structure and function of the skin and hair, provided that the effect is ''mild'' and provides for a third ''quasi-drug'' category of product accommodating ''mild,'' borderline physiological effects, such as hair-growth promoters [50a]. However, initiatives currently underway in Japan promise to alter the regulation of cosmetics by shifting to a postmarketing system more nearly aligned with those in effect in the U.S. and E.U. [50b]. Some regulatory systems currently reflect features of both the U.S. and EU systems; this is true, for example, of the system operative in Canada [50c]. In some cases, the concept of a regional consortium is being employed to facilitate international cooperation (such as the Andean Pact and Mercosur groups of nations in South America) [50d,e]. Still other third-world national regulatory systems are currently being updated, often using the U.S. or EU regulatory systems as models, to afford their citizens increased levels of protection.

The unprecedented growth experienced by the cosmetic industry in the 1980s and 1990s has also had its impact on international cosmetic regulation. Corporate consolidations and acquisitions of American companies and domestic product brands by foreign-based corporations have refashioned the concept of multinational corporations. The economic imperatives of these new ''world-class'' companies—to expand market penetration and market share in global overseas markets—have resulted in regulatory challenges in the international marketplace.

The modification of existing legislation that is viewed as an impediment to international trade, with a goal of alignment and harmonization of national laws and cosmetic regulations, has emerged as a central tenet of recent and current international negotiations. Hendrick and Horton [51] observe that:

> Precisely because the regulatory requirements of different countries vary considerably, harmonization of regulations among countries is a worthy goal. As we move toward a global economy with more countries placing an emphasis on imports and exports, harmonization would assist in the reduction of barriers to trade.

The United States, a member of the World Trade Organization (WTO) since its formation in 1995, is a signatory to two principal international trade agreements that are relevant to the marketing of cosmetics and other FDA-regulated products: the General Agreement on Tariffs and Trade (GATT) and the North American Free Trade Agreement (NAFTA). Both the GATT and NAFTA Agreements contain separate agreements on Technical Barriers to Trade (TBT) and Sanitary and Phytosanitary Measures (SBS), whose provisions seek to eliminate regulations, product standards, and procedures that constitute artificial technical barriers to trade. Both, however, also reserve to sovereign signatory states the right to determine whatever level of public health protection they believe necessary for the benefit of their citizens, agriculture, and environment. In the United States, these initiatives have become important ''pillars'' of the Vice President's *National Performance Review (NPR)*, and the FDA, as an agency of the executive branch, has fully supported these initiatives across all agency programs.

The FDA's policy on the international harmonization of regulatory requirements and guidelines was published in the *Federal Register* in 1995 [52]; additionally, Section

410(b) of the 1997 FDA Modernization Act (FDAMA) requires that the FDA support the Office of the U.S. Trade Representative (USTR) in meeting with other countries for the purposes of harmonizing regulatory approaches and achieving mutual recognition agreements, to the extent harmonization continues the consumer protections consistent with the FD&C Act [52c]. Agency goals are to simultaneously facilitate international trade and promote mutual understanding, while protecting national interests and establishing a model for resolving issues on the basis of sound scientific evidence in an objective atmosphere. The agency is committed to working toward facilitating the exchange of scientific and regulatory information and knowledge with foreign government officials, and accepting the equivalent standards, compliance activities, and enforcement programs of other countries, provided that the FDA is satisfied such standards, activities, and programs meet the FDA's level of public health protection. However, the FDA is equally committed to the thesis that harmonization activities must not result in a lowering of the gate to furtherance of public health protections afforded by U.S. law (e.g., ''downward harmonization'').

The FDA Office of Cosmetics and Colors (OCAC), which is responsible for administering the cosmetics provisions of the FD&C Act, is committed to seeking implementation of the U.S. Government policies on international harmonization. Outreach conferences with regulatory authorities in Israel, the Andean Pact nations, the EU, Canada, Japan, China, and others have sought to achieve international harmonization through identifying areas of commonality among the regulatory schemes in the various administrations, rather than hoping to arrive at a single global regulatory structure. In particular, two quadrilateral *Cosmetic Harmonization and International Cooperation (C.H.I.C.)* conferences between the United States, the European Union, Canada, and Japan, held in 1999 and 2000, have identified a number of areas of mutual interest, concerning which discussions are continuing at the present time; these areas of mutual interest include:

Memoranda of cooperation (MOC)
Regulatory reform
Animal testing
Cosmetic ingredient nomenclature
Approved color additives
Sunscreens
Drug–cosmetics and quasi-drugs
Safety substantiation
Fragrance allergenicity
International adverse event safety ''alert system''

Further details about the second C.H.I.C. meeting are posted on the FDA's website at the Cosmetics Program Homepage (*http://www.cfsan.fda.gov/cosmetics.html*).

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DISCLAIMER

The views expressed herein are those of the authors and do not necessarily represent those of the FDA.

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Legislation in Japan

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REGULATORY ENVIRONMENT

The cosmetic regulations in Japan are extensive and complex [1]. The legal classification of topically applied products is different from the United States and the European Union, where they are divided into only two categories: drugs and cosmetics. In Japan, there are additional regulations covering cosmetic products with pharmacological action, called quasidrugs, which are ranked between cosmetics and drugs [2]. Under the Pharmaceutical Affairs Law, cosmetics, as well as drugs and quasidrugs, are also subject to premarket clearance by the Ministry of Health and Welfare (MHW) [1]. The definitions of drugs, cosmetics, and quasidrugs in the regulations [3] read as follows:

Drugs are defined as:

1. Articles recognized in the official Japanese Pharmacopoeia.
2. Articles (other than quasidrugs) that are intended for use in the diagnosis, cure, or prevention of disease in man or animals, and that are not equipment or instruments (including dental materials, medical supplies, and sanitary materials).
3. Articles (other than quasidrugs and cosmetics) that are intended to affect the structure or any function of the body of man or animals, and that are not equipment or instruments (Paragraph 1, Article 2 of the Law).

Quasidrugs are articles that have the purposes given as follows and exert mild actions on the human body, or similar articles designated by the Minister of Health and Welfare. They exclude not only equipment and instruments, but also any article intended, in addition to the following purposes, for the use of drugs previously described in (2) and (3).

1. Prevention of nausea or other discomfort, foul breath, or body odor.
2. Prevention of prickly heat, sores, and the like.
3. Prevention of hair loss, restoration of hair, or depilation of unwanted hair.
4. Killing or prevention of rats, flies, mosquitoes, fleas, etc. for maintaining the health of man or animals (Paragraph 2, Article 2 of the Law).

Quasidrugs designated by the Minister of Health and Welfare (Notification No. 14, 1961), include cotton products intended for sanitary purposes (including paper cotton), as well as the following products with a mild action on the human body:

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1. Hair dyes
2. Agents for permanent waving
3. Products that combine the purposes of use as stipulated in Paragraph 3, Article 2 of the Law (on cosmetics), with the purposes of prevention of acne, chapping, itchy skin rash, chilblain, etc., as well as disinfection of the skin and mouth
4. Bath preparations

Among the products just described, the third category comprises the so-called medicated cosmetics.

The term ''cosmetics'' means any article intended to be used by means of rubbing, sprinkling, or by similar application to the human body for cleaning, beautifying, promoting attractiveness, altering the appearance of the human body, and for keeping the skin and hair healthy, provided that the action of the article on the human body is mild. Such articles exclude the articles intended, besides the aforementioned purposes, for the use of drugs previously described in (2) or (3), and quasidrugs (Paragraph 3, Article 2 of the Law).

COSMETICS

At each stage of development, manufacture/import, distribution, and use, the prescribed regulations are put into practice, including systems of the examination for approval, manufacture/importation, distribution control, and postmarketing surveillance, respectively [3].

Procedures for premarket clearance have been simplified. As a series of steps for streamlining the cosmetic approval and licensing system, cosmetics using ingredients listed in the Comprehensive Licensing Standard of Cosmetics by Category (CLS) and that are in compliance with the Standards established, do not require approval but require a license by category (Table 1) [4–6]. Licensing will be granted by category according to the CLS [7]. As for the cosmetic product category, there were 35 separate categories at one time. These were reduced to 25 in 1994 and integrated into 11 in 1997 (Table 1) [6]. Additions to and review of the cosmetic ingredients list have recently been made almost at annual intervals. On the other hand, cosmetics using ingredients that are not in compliance with the CLS require approval by category, and a prior evaluation is conducted of the particulars indicated in the application filed for approval [4,5]. The following cosmetics are included in this group [7]:

- Cosmetics containing new ingredient or ingredient not listed in the CLS.
- Cosmetics containing ingredient in a larger quantity exceeding the upper limit specified in the CLS.
- Cosmetics containing ingredient not listed in the intended category of the CLS, but in another category of the CLS.
- Cosmetics whose method of use, etc., are clearly different from the cosmetics defined in the CLS.
- Cosmetics containing hormones; these products are not included in the CLS, and an application for approval must be made.

The following data must be attached to the application where appropriate (these are especially required for cosmetics containing a new ingredient):

TABLE 1 The Categories of Cosmetic Products

Categories	Definition of the products
Cleansing preparations	Exclusively used for cleansing
Haircare preparations	Exclusively used on the hair and scalp
Treatment preparations	Used for keeping the skin healthy
Makeup preparations	Mainly used for makeup effect
Fragrant preparations	Liquid, powdered, and other fragrance products aimed at providing scent; fall under the classification of ''perfumes''
Suntan and sunscreen preparations	Exclusively used for tanning or sunscreening
Nail makeup preparations	Exclusively used for protecting nails, makeup effect on the nail, or are used for removing nail enamel
Eyeliner preparations	Used for makeup effect on the eyelids by using them along the hairline of eyelashes
Lip preparations	Exclusively used for makeup effect on the lips or are used for protecting lips
Oral preparations	Used for cleansing the mouth or preventing halitosis
Bath preparations	Used to cleanse the body and to enjoy the fragrance; used by placing them into a bathtub or by other similar action

Source: Ref. 6.

- Origin and background of discovery
- Previous use in foreign countries
- Characteristics and comparison with other cosmetics
- Determination of chemical structure
- Physicochemical properties
- Safety

In the case of cosmetics containing liposomes, the data attached to the application should include the stability of the liposome during product distribution and safety.

QUASIDRUGS

In the Pharmaceutical Affairs Law, quasidrugs are defined as articles having ''fixed purpose of use'' and ''mild action on the body,'' or similar articles designated by the Minister of Health and Welfare. Most of the products in this category are what we call ''pseudodrugs'' or ''cosmeceuticals,'' a current definition of which would be ''those products that will achieve cosmetic results by means of some degree of physiological action'' [8]. The defined quasidrug products include mouth refreshers, body deodorants, talcum powders, hair growers, depilatories, hair dyes, permanent waving products, bath preparations, medical cosmetics (including medical soaps), medicated dentifrices, and so on [3,9].

At each stage of development, manufacture/import, distribution, and use, the prescribed regulations are enforced [3]. Manufacturers of quasidrugs are required to obtain government approval before marketing. Approval of a product under an application for manufacturing/importing is the responsibility of the MHW. Is it adequate as a quasidrug in view of its efficacy, safety, etc.? Therefore, the examination procedures for approval as well as the data and documentation required to be submitted for filing an application

differ with the indications and effects of each product [3]. The following data must be attached according to the kind of ingredients employed, and so on:

- Origin, background of discovery, use in foreign countries, etc.
- Physicochemical properties, specifications, testing methods, etc.
- Stability
- Safety
- Indications or effects

The scope of the data to be attached to the application depends on the type of quasidrug; (1) new quasidrugs that obviously differ from any previously approved products with respect to active ingredients, usage and dosage, and/or indications or effects; (2) quasidrugs identical with previously approved quasidrug(s); or (3) other quasidrugs that are other than those specified in (1) and (2) [3].

All products for approval as a quasidrug must be within the scope stipulated by the Pharmaceutical Affairs Law. Thus, approval of a product as a quasidrug is determined by an integrated judgement of various factors such as its ingredients, quantity (composition), indications and effects, usage and dosage, and dosage form. For example, those products whose effects are not mild—hence, coming under the category of poisons or deleterious drugs—are not approved even if their indications and effects and dosage forms are within the scope of the quasidrugs legislation. Likewise, products for which the intended use deviates from the scope of quasidrug are also not approved even if their effects are mild [3].

COSMETICS IN THE FUTURE

The Japanese Government sets objectives to relax or abolish many of the current regulatory items in various industries. As a part of these plans, cosmetic deregulation has been progressing based on the government's policy to review current licensing systems and ingredient labeling controls [10]. A committee, which was organized on the basis of a plan drafted by the government, was commissioned in order to figure out how to bring about a deregulated domestic market and a harmonized international market [11]. On March 31, 1997 the future direction and issues to be addressed in connection with cosmetic regulations were set out by the committee in the form of an interim report [4]. The following is an outline that indicates the shift of the regulatory system to one based on the manufacturers' self-responsibility, basically similar to that of the European Union and the United States [4,10].

1. Ingredient substance controls: Recompilation of the Negative List, the Positive List, and the Existing List of Ingredient Substances in order to abolish the current premarketing licensing systems.
2. Licensing systems for companies manufacturing and importing cosmetics: Maintenance of current systems in principle, while establishing new quality-control systems and simplifying requirements for license approval.
3. Ingredients labeling control: Creation of regulations that force cosmetic manufactures and importing companies to include all ingredients on the label in order to give consumers sufficient information to help them evaluate and select the cosmetics.
4. Promotion of the appropriate uses of cosmetics, and collecting and releasing to the public information on the safety of cosmetics.

After investigation by the working group on the specific issues indicated by the interim report, the committee has issued a final report. The report is entitled ''How cosmetic regulations should be in the future'' and consists of three parts [4,5]; 1) background of discussions on cosmetic regulation, 2) desired future regulations and specific handling procedure, and 3) issues remaining to be addressed.

The main points of the second part (desired future regulations and specific handling procedure) are as follows:

(1) Ingredient Control. It is appropriate to control the use of the ingredients through a list of prohibited and restricted ingredients (Negative List), and by doing so to abolish the approval system by category, as well as to control specific ingre-

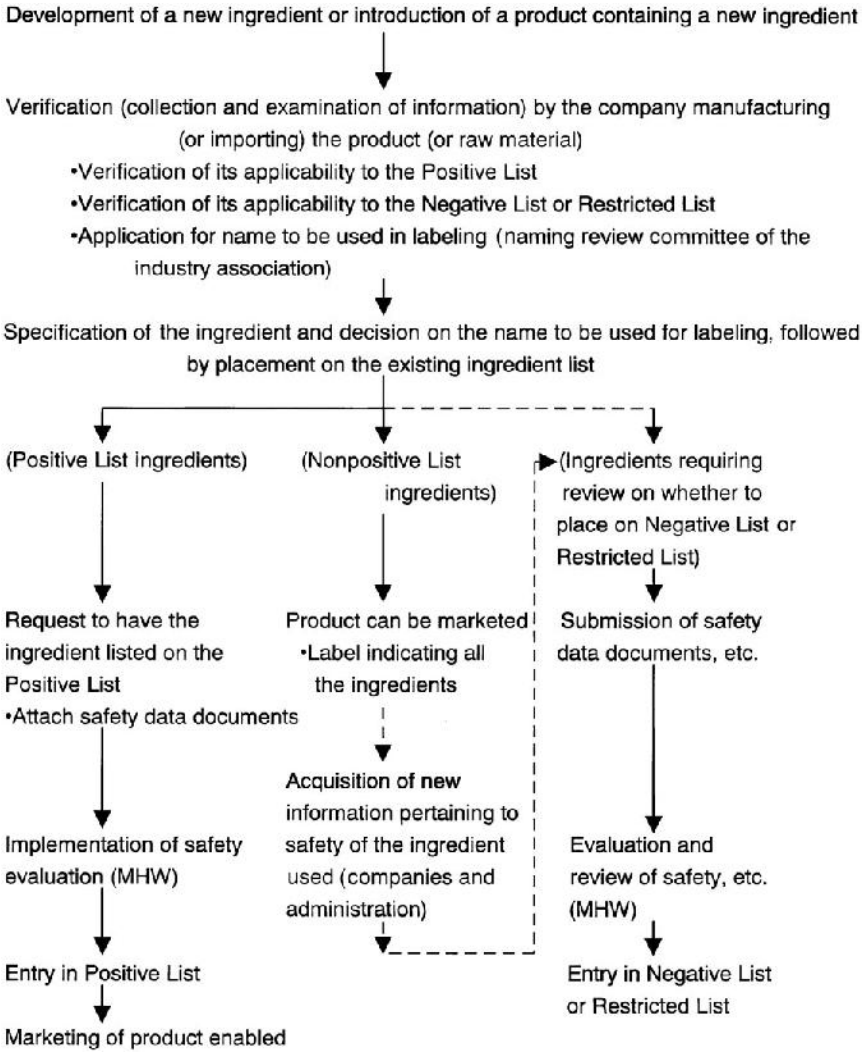

FIGURE 1 Flow chart of the procedure for treating new ingredients for cosmetics. (From Refs. 4 and 5.)

dient groups (preservatives, UV absorbents, coal tar colors) that require cautious handling under appropriate safety evaluation, by drawing up a list of ingredients that may be used in formulations (Positive List). As for the new ingredients, the procedure for introducing them shall be as indicated on the flow chart shown in Figure 1 [4,5].

(2) Licensing System. A manufacturing or importing licensing system should be maintained.

(3) Regulations on Ingredient Labeling. As it is important to provide adequate information to consumers to facilitate their selection and verification of a product, in principle an ''all-ingredient labeling system'' shall be adopted for ingredients used in formulations.

(4) Cosmetic information, etc.

The MHW is now studying the possibility of amending the law and regulations in order to implement the new system by fiscal year 2000 according to the final report.

QUASIDRUGS IN THE FUTURE

There has been a great demand by consumers for innovative cosmetic products with pharmacological action, i.e., pseudodrugs or cosmeceuticals such as skin antiaging products. To satisfy their demands, research on the skin has been undertaken to develop new active ingredients for skin antiaging products. How should those products be legally categorized? Quasidrugs would seem to be suitable for such products to be categorized. However, all of the products have not always been approved as quasidrugs to date. Taking antiwrinkle products, for example, no new products have been approved under the existing quasidrug specifications.

Generally, topically applied quasidrugs are intended to mollify unwanted aspects of the skin and have a mild action on the human body, whereas medical drugs are intended to treat specific diseases. Therefore, hair-growth products with a mild action on male-pattern baldness, which is not a disease [2], are quasidrugs. On the other hand, products intended for alopecia areata, which is a disease, are regarded as drugs. The natural aging of skin, like wrinkling, is not a disease, for example. We should also keep in mind that ''high efficacy'' should not always involve ''strong action.'' There will be many pseudodrugs or cosmeceutical products with mild actions showing good efficacy.

Legally, the Minister of Health and Welfare can add new, novel types of products to the current list of types of quasidrugs [12]. Therefore, we hope that before long the aforementioned new products will be listed as quasidrugs.

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