1

General and Legal Aspects of Cosmetics

1.1 Short Look at the History of Cosmetics

The term cosmetic, originated from the ancient Greek word meaning "order or decorate," refers to the body and beauty care. This includes the maintenance, restoration, and enhancement of the beauty of human body. The first sign of cosmetics dated back about 10 000 BCE. The Mesolithic people applied grease and castor oil to soften their skin. They painted tattoos with plant dyes. About 7000 years later (3000 BCE), Egyptian parchment described the use of creams to sooth the skin and reduce wrinkles [1]. In the ancient Near East, men applied oils to their hair and beard. Women used eye paints, rouge, powders, and ointments on their body. In 50 BCE, Cleopatra was not only known as a beauty but also known for her intensive use of cosmetics. She possessed many products from nature such as beeswax, honey, and natural oils as well as products made from fruits, vegetables, herbs, and seeds, besides eggs and milk. She bathed in goat milk for skin regeneration. At that time, there were mirrors, makeup, makeup containers, combs, wash dishes, wigs, as well as tweezers and blades for removal of unwanted hair. Vermilion and red ocher were used for coloring the lips and cheeks; henna was used for coloring the hair, skin, toenails, and fingernails; and the malachite green, gray galena, and finely ground antimony were used for eyes as an eyeliner. The Greek physician Galen (about 200 CE) developed the first cold cream from beeswax, olive oil, and water [1]. The Romans introduced communal baths for noble persons. In the Middle Ages, they used hair dye and makeup, in addition to natural skin care and herbal remedies. During those times, a pale complexion was considered beautiful. With white lead, they achieved a flawless pallor. This substance and other cosmetics are highly toxic and often caused abscesses that did not heal. During the Renaissance, the Venetians dyed their hair using plant colors, fixed with clay, and baked in the sun. When it came to Elizabeth I of England (about 1580) and Catherine de Medici in France, dyeing of the cheeks and lips became popular again. The red lip color came from cochineal, a red dye from the cochineal scale insect. In the eighteenth century, bismuth oxide, mercury oxide, tin oxide, and talc were used to whiten the skin. Red makeup for the lips and cheeks emerged from safflower, cochineal, redwood, sandalwood, and vermilion. In addition, the hair was treated with greasy pomades. The hair powder consisted mostly of wheat or rice starch, partly colored. At present, there are

Cosmetic Creams: Development, Manufacture and Marketing of Effective Skin Care Products,
First Edition. Wilfried Rähse.

ranges of cosmetic products that have been tested for their safe use. The aim has not changed in thousands of years. Primarily, cosmetics mean increasing attractiveness by beautifying the body and face. For a closer look at the historical processes, the following references are suitable [2–4].

1.2 Definition of Cosmetics

The legal text of the European Cosmetics Regulation [5] defines what a cosmetic product is and forms the legal basis in the European Community (EC) for the delimitation to the medical and therapeutic agents. This is the text of (EC) No. 1223/2009, Article 1a (quote): "Cosmetic Product agent any substance or mixture intended to be placed in contact with the external 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, protecting them, keeping them in good condition or correcting body odors."

A very similar definition is given in the German LFGB regulation of 2005 (Lebensmittel-, Bedarfsgegenstände-, und Futtermittelgesetzbuch [6]). Text of (GER) LFGB §2, Article 5 (translation): "Cosmetic agents are substances or mixtures of substances exclusively or predominantly intended to be applied externally to the body of the human being or in his oral cavity for cleansing, protecting, maintaining a good condition, for perfuming, changing the appearance or to influence the body odor. Cosmetics are not substances or mixtures of substances which are intended to influence the body forms."

Already, the revision of the Federal Food, Drug, and Cosmetic Act (FD&C Act) of 1938 described the intended use of these products in a wording [7, 8] that is valid until now: (USA, Food and Drug Administration [FDA]) …"(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, …" Among the products included in this definition are skin moisturizers, perfumes, lipsticks, fingernail polishes, eye and facial makeup preparations, cleansing shampoos, permanent waves, hair colors, and deodorants, as well as any substance intended for use as a component of a cosmetic product.

Essentially, the purpose of applying cosmetics is to increase the attractiveness of the user. This goal is achieved with many cosmetic products: unobtrusive, barely perceptible in the daily cleaning of skin and hair as well as the teeth, or eye-catching for decorative cosmetics, hair styling or coloring. To maintain the good condition, the daily use of cosmetic products on the skin and in the oral cavity is necessary; this applies with restrictions also for the hair (nose and ears are not mentioned in the regulation). The main tasks of cosmetics are cleansing, beautifying, perfuming, protecting, and maintaining a good condition of skin, nails, hair, and the teeth.

Healing and elimination of skin damage, infections, and diseases are the tasks of the therapeutic agents and are subject to other legal regulations. However, many active ingredients that are often used in cosmetic creams form a potential

for conflict because they have a therapeutic effect in addition to the cosmetic (see Section 1.10). For example, dexpanthenol is not only a good moisturizing agent but also accelerates healing of wounds (pharmacy product: Bepanthen). Hemp oil, a good skin oil from nature with a skin-like C-chain distribution, is known (in Russia) for its healing effect of inner throat problems. Natural jasmine oil from Egypt has a very pleasant scent. Inhaling of this oil resulted in a proven relaxation of the body and used to facilitate birth in earlier days. There are many substances that show two or three effects, of which at least one is not a part of cosmetics. For cosmetic products, these available effects are not allowed to be labeled on the packaging as an advantage.

1.3 Typical Cosmetic Products

The product groups, which belong to the cosmetics, comprise the areas of hands, nails, arms, armpits, feet, legs, body and hair, face, eyes, lips, mouth, and teeth as well as the external genital areas. A concise overview of products in categories of cosmetics, summarized after application, and some product examples can be found in Table 1.1. Skin creams, which are the main focus here, belong to the first category "Skin cleansing and care."

Table 1.1 Typical cosmetic products.

Category/ Application	Products	Examples
Skin cleansing and care	➢ Soap, cleansing milk, facial fluid, -foam, -oil, mask, cleaning water, -lotion, -oil, hair and body wash, perfume and bubble baths, shower gel, bathing accessories ➢ Eye and face cream, -lotion, -emulsion, moisturizer and antiaging, facial concentrate (serum), eye patches, body lotion and cream, hand and foot cream, gels, masks, lip balm, genital cream ➢ Shaving cream, shaving soap, aftershave ➢ Depilatories ➢ Sunscreen milk, sunscreen lotion, water-repellent lotion, repellents (insects)	
Dental and oral care	➢ Toothpaste with different promises, powder, gel, dental floss, toothbrush, mouthwash, tongue cleaning ➢ Dentures[a]: cleaning by toothpaste, tab or powder and adhesion with a special cream	

(Continued)

Table 1.1 (Continued)

Category/ Application	Products	Examples
Hair treatment	➢ Shampoo, dry shampoo, styling, conditioner, hair care spray, permanent wave, hair gel, fluid, cream, foam, hair oil, mask, spray, hair color, hair tint, powder, hair care, serum, balsam, wax, hair tonic, antidandruff, pomade, hair perfume	
Decorative cosmetics	➢ Makeup, -remover, rouge, powder, -cloth, foundation, concealer, highlighter, primer, mascara, eye shadow, eye gel, eyeliner, eye pencil, eye brow pencil, eyebrow gel, eyelash care, lipstick, lip gloss, lip contour pin, nail polish, -remover, nail top coat, artificial nails, foundations, brushes ➢ Self-tanners	
Scent, smell	➢ Eau de perfume, eau de toilette, eau de cologne, deodorant, anti-perspirant	

a) Medical device.
Source: Courtesy of Douglas.

1.4 Legal Regulations of Cosmetics in Europe

Cosmetic products must meet a number of legal requirements from the European Union (EU) and the national parliaments, before they can be marketed. In Europe, the development, production, and marketing of cosmetic products are regulated by the **Cosmetics Regulation (EC) No 1223/2009** [5]. In addition, in Germany, the Cosmetics Ordinance (Kosmetik Verordnung) [9] and the Food and Feed Code (LFGB) of 2005 govern the trade of cosmetic products (§ 2 (5), § 26–29) [6] and others. All must be observed. Supplementary EC directives exist for the production of cosmetics, namely the GMP (Good Manufacturing Practice) Guidelines and the EHEDG (European Hygienic Engineering and Design Group) Guidelines, which are discussed in Chapter 11.

The most important basis in all EC Member States is the aforementioned Cosmetics Regulation, which has entered into force on 11 January 2012 as the successor to Directive 76/768 EEC. The new version of the German Cosmetics Ordinance has been in force since 24 August 2014. It takes over the EC Regulation and additionally regulates the information obligation; the use of the German language, information, and treatment centers for poisoning; exceptions for importation; and sanctions in the case of violation of the regulation.

Table 1.2 Structure of the Regulation (EC) No 1223/2009 on cosmetic products.

Chap.	Titles	Articles
I	SCOPE, DEFINITIONS	1 Scope and objective; 2 Definitions
II	SAFETY, RESPONSIBILITY, FREE MOVEMENT	3 Safety; 4 Responsible person; 5 Obligations of responsible persons; 6 Obligations of distributors; 7 Identification within the supply chain; 8 Good manufacturing practice; 9 Free movement
III	SAFETY ASSESSMENT, PRODUCT INFORMATION FILE, NOTIFICATION	10 Safety assessment; 11 Product information file; 12 Sampling and analysis; 13 Notification
IV	RESTRICTIONS FOR CERTAIN SUBSTANCES	14 Restrictions for substances listed in the Annexes; 15 Substances classified as CMR substances; 16 Nanomaterials; 17 Traces of prohibited substances
V	ANIMAL TESTING	18 Animal testing
VI	CONSUMER INFORMATION	19 Labeling; 20 Product claims; 21 Access to information for the public
VII	MARKET SURVEILLANCE	22 In-market control, 23 Communication of serious undesirable effects; 24 Information on substances
VIII	NON-COMPLIANCE, SAFEGUARD CLAUSE	25 Non-compliance by the responsible person; 26 Non-compliance by distributors; 27 Safeguard clause; 28 Good administrative practices
IX	ADMINISTRATIVE COOPERATION	29 Cooperation between competent authorities; 30 Cooperation regarding verification of product information files
X	IMPLEMENTING MEASURES, FINAL PROVISIONS	31 Amendment of the Annexes; 32 Committee procedure; 33 Glossary of common ingredient names; 34 Competent authorities, poison control centres or assimilated entities; 35 Annual report on animal testing; 36 Formal objection against harmonized standards; 37 Penalties; 38 Repeal; 39 Transitional provisions; 40 Entry into force and date of application

Source: Data from Ref. [5].

The structure of the Cosmetics Directive is reproduced in Table 1.2. On the one hand, it determines the substance approval, describes in detail the prohibited and restricted use of substances, also of the dyes, ultraviolet (UV) filters and preservatives, all listed in the annexes (Table 1.3). On the other hand, the directive demands some quality checks, a qualified safety assessment of the formulation (see Chapter 13), and production according to the GMP standard (Chapter 11). The elaboration of a qualified safety assessment of the ingredients and the entire formulation needs an academically trained expert, who has gained knowledge by studying in a related field and having a maximum experience in this field.

For all cosmetic products, the current version of the Cosmetics Regulation in accordance with Article 11 requires a "Product Information File" (P.I.F.).

Table 1.3 Annexes of the Directive (EG) Nr. 1223/2009 on cosmetic products [5].

Annex	Titles	Subjects
I	COSMETIC PRODUCT SAFETY REPORT	PART A – Cosmetic product safety information; PART B – Cosmetic product safety assessment
II	LIST OF SUBSTANCES PROHIBITED IN COSMETIC PRODUCTS	1338 identified prohibited substances
III	LIST OF SUBSTANCES WHICH COSMETIC PRODUCTS MUST NOT CONTAIN EXCEPT SUBJECT TO THE RESTRICTIONS LAID DOWN	256 substances which may be used up to a maximum value
IV	LIST OF COLORANTS ALLOWED IN COSMETIC PRODUCTS	153 allowed colorants
V	LIST OF PRESERVATIVES ALLOWED IN COSMETIC PRODUCTS	57 preservatives which may be used up to a limit value
VI	LIST OF UV FILTERS ALLOWED IN COSMETIC PRODUCTS	28 substances of limited concentration in ready for use preparation
VII	SYMBOLS USED ON PACKAGING/CONTAINER	Period-after-opening; Date of minimum durability
VIII	LIST OF VALIDATED ALTERNATIVE METHODS TO ANIMAL TESTING	
IX		PART A – Repealed Directive with its successive amendments; PART B – List of time-limits for transposition into national law and application

This report must be elaborated by an expert and provided at the request of an authority. Quote of Article 11: "…When a cosmetic product is placed on the market, the responsible person shall keep a product information file for it. The product information file shall be kept for a period of ten years following the date on which the last batch of the cosmetic product was placed on the market…." The most important part of P.I.F. represents the Cosmetic Product Safety Report (CPSR) or Safety Assessment. If not included in the CPSR, a product description must be prefixed, and the production according to GMP guidelines must also be confirmed (Chapter 13). A promised, specific effect or performance requires proof of the effect. For example, it is necessary for sun creams to determine the sun protection factor (SPF), which indicates the reliable effect by a certified method (ISO Standard – ISO 24444-2010). The last point of the P.I.F. need not be mentioned further because cosmetic companies do not carry out animal testing. If this is exceptionally not the case, the cosmetic regulation provides accurate information.

1.5 Label Lettering and Trademark

Various information for the consumer must be given on the packaging. Table 1.4 contains the hints for a label that needs to be checked point by point. For example, the label must include a product description in keywords and a list of ingredients in the INCI nomenclature (International Nomenclature of Cosmetic Ingredients). In addition, an instruction for the intended use with possible hazard warnings (for example, restrictions on children) as well as information about the content and durability of the product should be listed. The Directive requires the easy-to-read indication of the responsible company (with address) on the packaging. If products are made according to the (EC) No 1223/2009, this guarantees free movement of cosmetic products within the European market and ensures a high level of protection for human health under normal or foreseeable conditions of use.

Figure 1.1 demonstrates how the label might look on a cosmetic jar, pot, or dispenser. Within the limited space on the label, all legal requirements must be met, with the font clearly legible. On the front of the packaging, the brand name and logo (trademark) in brand-typical colors are usually found, including the function and application of the content. Instructions, a brief description of the likely effect, ingredients, and further details of the product as well as the content (volume or mass) and the manufacturer details can be found on the back of the

Table 1.4 Labeling of cosmetic products according to the Cosmetics Regulation (EC) No 1223/2009.

General instructions
➢ Name and address of the manufacturer or of person responsible for marketing the product;
➢ The nominal contents at the time of packaging, by weight or by volume;
➢ Date of minimum durability indicated for products with a minimum durability of less than 30 months;
➢ Period of time after opening the package for which the product can be used; valid for products with a minimum durability of more than 30 months (indicated with the symbol representing an open pot);
➢ Function of the product and particular precautions for use;
➢ Batch number of manufacture;
➢ Perfume and aromatic compositions and their raw materials shall be referred to by the terms “parfum” or “aroma”;
➢ Special rules for nanomaterials;
➢ Serious product claims;
Some countries require additional statements such as
➢ Storage: 4–22 °C;
➢ No animal tests
List of ingredients: INCI = International Nomenclature of Cosmetic Ingredients
➢ Order of the ingredients according to their mass proportions (highest percentage first)
➢ Ingredients less than 1% in any order
➢ INCI-specification: Parfum or Aroma; however, 26 fragrance allergens must be declared from a certain amount (Section 9.8)
➢ The CI-number specifies the dyes

CI, color index.

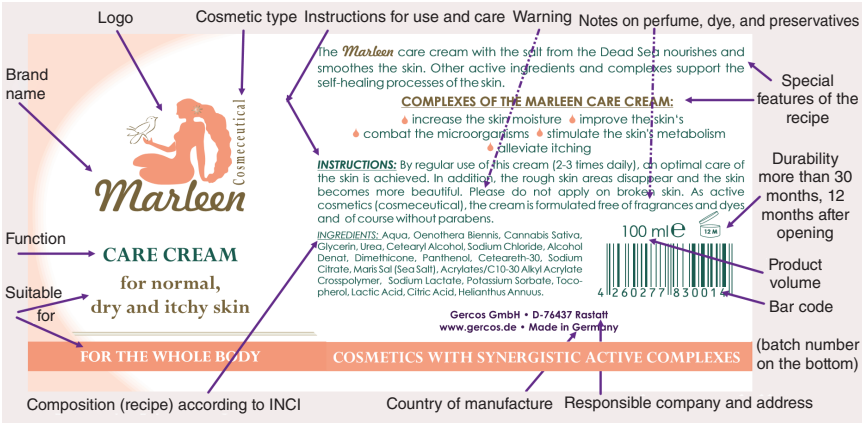


Figure 1.1 Lettering of the label according to the cosmetics regulation; this label is glued on a round dispenser.

packaging. The company name and postal address are sufficient to identify the person responsible for placing the goods on the market. The Internet address (website) provides further information about the product, its application, and the ingredients. Through the imprint of the website, the name of the managing director, the exact address of the company, and the telephone number can be found.

Furthermore, a batch number and the indication of the minimum durability are required on the packaging (e.g. best used before the end of March 2021), except for cosmetic products with a minimum durability of more than 30 months. For such products, an indication of the period after the opening must be given for which the product is safe and can be used without any harm to the consumer. This instruction requires the use of a picture from the Cosmetics Regulation (Annex VII, 2). The image shows an open pot with a figure that indicates the durability in months as shown in Figure 1.1.

In addition to the Cosmetics Ordinance, other laws must also be observed for the information on packaging and for the marketing. Especially in Germany, the Remedies Advertising Act ("Heilmittelwerbegesetz" HWG from 1965, last updated 2015 [10]) restricts advertising claims. This Directive prohibits statements on the label for the detection, elimination, or alleviation of illnesses; ailments; body damage; or morbid complaints. In addition, Directive 2005/29/EC of the European Parliament and of the Council (11 May 2005), concerning unfair business-to-consumer commercial practices in the internal market, provides that the Community works according to the same regulations and contribute to a high level of consumer protection.

New products or product groups sometimes require a new brand. Searching and finding a new brand name and an excellent logo is not easy. The brand should be memorable, easy to pronounce, and distinctive, even in other languages, and should be clearly and positively different from the competition. After finding a good name or a letter combination with logo, a national application is

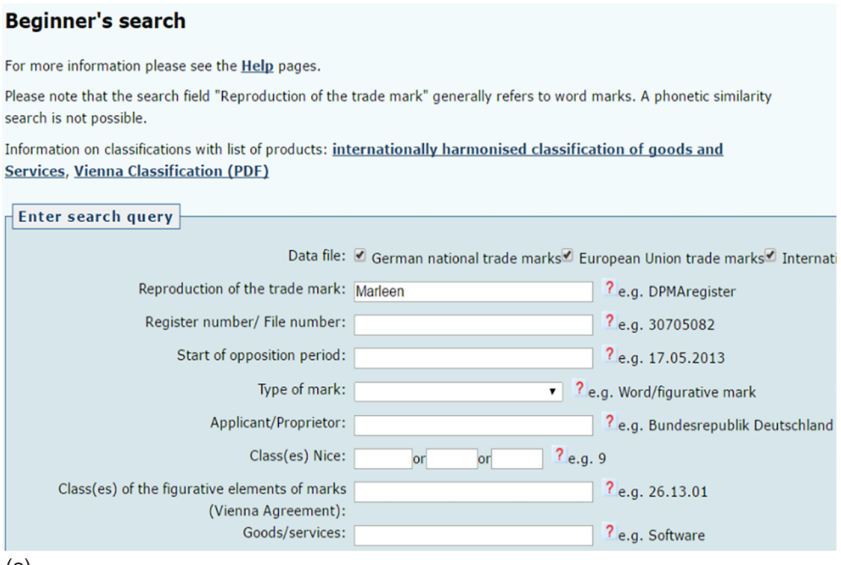
recommended at the Patent and Trademark Office (in Germany: DPMA [11]) or even a European application at the EUIPO (European Union Intellectual Property Office in Alicante, Spain [12]). Protected trademarks may not be used by competitors in the respective countries. The new mark name must be free, i.e. without registration in the own business area. The use of an already registered trade name or a very similar name in the same business area may result in a chargeable warning of the name holder. The owner prohibits the use of his brand name and demands the removal of all market products with this name. The withdrawal of products may result in high costs, which can be avoided. In order to ensure whether a brand name has already been given, it is worth taking a look at the national trademark registries [11], before printing the labels.

In most cases, brands consist of words and/or images or image with letters. However, they can also be three-dimensional, color, and sound brands. The definition of a trademark can be found in Article 2, Directive 2008/95/EC of the European Parliament and of the Council [13]. Quote: "A trade mark may consist of any signs capable of being represented graphically, particularly words, including personal names, designs, letters, numerals, the shape of goods or of their packaging, provided that such signs are capable of distinguishing the goods or services of one undertaking from those of other undertakings."

The national brand register, here the German Patent and Trademark Office (DPMA), precisely shows which mark names and logos are registered and protected in Germany, in the EU, and worldwide. Less significant is the search at the EUIPO because it provides only hits of European registrations. However, it should be considered to complete the search for important brands outside their own national borders. The national trademarks apply to a single country, but EU registrations apply to all member countries. A search for brand names in the DPMA demonstrates the example shown in Figure 1.2, which continues the representation of Figure 1.1. The company that brings the product into the market is mentioned on the label of the packaging.

Before marketing, the company's managing director and his experts must ensure that all measures are implemented in accordance with the EC Directive, especially

- Check all ingredients of the formulation (allowed, maximum application quantity)
- Specify the ingredients in INCI nomenclature and sequence
- The full details printed on the label and package (function of the product, claims, usage, warnings [if necessary], nanoparticles used, volume, date and time of durability, batch number, and manufacturer's address)
- The production according to the GMP standard
- Quality check of the product
- Detailed safety assessment and summary
- Registration of the product at the Cosmetic Products Notification Portal (CPNP) (see Section 1.6)
- Completed P.I.F.



Beginner's search

For more information please see the **Help** pages.

Please note that the search field "Reproduction of the trade mark" generally refers to word marks. A phonetic similarity search is not possible.

Information on classifications with list of products: **internationally harmonised classification of goods and Services**, **Vienna Classification (PDF)**

Enter search query

Data file:	☑ German national trade marks ☑ European Union trade marks ☑ Internat
Reproduction of the trade mark:	Marleen — e.g. DPMAregister
Register number/ File number:	e.g. 30705082
Start of opposition period:	e.g. 17.05.2013
Type of mark:	e.g. Word/figurative mark
Applicant/Proprietor:	e.g. Bundesrepublik Deutschland
Class(es) Nice:	or or e.g. 9
Class(es) of the figurative elements of marks (Vienna Agreement):	e.g. 26.13.01
Goods/services:	e.g. Software

(a)

Database response

No.	Selection	Data file	File number/Register number	Reproduction of the trade mark	Status of file
1	☐	DE	713127	Lilli **Marleen**	Trade mark registered
2	☐	DE	962791	Tilly-**Marleen**	File destroyed
3	☐	DE	1066893	**MARLEEN**	File destroyed
4	☐	DE	1132582	LILI **MARLEEN**	File destroyed
5	☐	DE	DD647222	LILI **MARLEEN**	File destroyed
6	☐	DE	DD648144	Marleen	Trade mark cancelled
7	☐	DE	395263433	Lili Marleen	Trade mark cancelled
8	☐	DE	304727326	LILI **MARLEEN**	Trade mark cancelled
9	☐	DE	306440121	Marie **Marleen** Die feine ART	Trade mark registered
10	☐	DE	307480682	SUNNY **MARLEEN**	Trade mark registered
11	☐	DE	3020100424680	Marleen Cosmeceutical	Trade mark registered
12	☐	DE	3020110100098	Lili **Marleen**	Trade mark registered

Clicking on this number leads to the trademark owner

(b)

Figure 1.2 Search of the brand name and logo in Germany via the DPMA register, the images show cutouts: (a) start of the search, (b) hits. Source: Data from Ref. [11].

1.6 Mandatory Registration of Cosmetic Products

The Cosmetics Regulation requires the product to be registered with the competent authorities. In Europe, the formulations must be electronically deposited with the CPNP. Quote of the CPNP [14]:

> The **Cosmetic Products Notification Portal** is a free of charge online notification system created for the implementation of Regulation (EC) No 1223/2009 on cosmetic products. When a product has been notified in the CPNP, there is no need for any further notification at national level within the EU. Regulation (EC) No 1223/2009 (Article 13) requires that the responsible persons and, under certain circumstances, the distributors of cosmetic products submit some information about the products they place or make available on the European market through the CPNP.
> The CPNP is making this information available electronically to:
>
> ✓ Competent Authorities (for the purposes of market surveillance, market analysis, evaluation and consumer information)
> ✓ Poison Centres or similar bodies established by EU countries (for the purposes of medical treatment)
> ✓ Cosmetic products responsible persons
> ✓ Distributors of cosmetic products.

1.7 Databases for Ingredients

For a complicated search for individual substances, the Annexes to the Cosmetics Regulation should not be used in the first step because "**CosIng**," the European Commission database [15], allows fast access to individual substances and their possible limitations according to the regulation. The database contains information on all cosmetic substances and ingredients used. CAS and EC numbers that identify the ingredient as well as the INCI names can also be found in CosIng. Permissible maximum amounts of the substance and the wording of warnings, which must be indicated on the packaging, are in the database. A check of the results with the Annexes of the Cosmetics Regulation whereby the search number can be taken from the CosIng answer is indispensable.

How the CosIng files look like is shown by two difficult examples. Sodium fluoride (Figure 1.3) represents the first example. This chemical substance is part of many types of toothpastes. In Germany, experts recommend to use the maximum permitted quantity. Sodium fluoride is toxic, for oral intake suffices 71 mg/kg body weight (LD_{LO}). Accordingly, a person weighing 60 kg may die after taking about 6 g of sodium fluoride. As it had been shown that the substance reduces caries formation, 1500 ppm F is allowed. By brushing the teeth twice a day and total swallowing of the foam, a 60 kg human would take about 6 mg, i.e. 1/1000 of the dangerous amount. However, the amount absorbed is more than a factor of less than 100, as the foam is spat out. The discussed limit values for children less than six years should be 500–700 ppm. The Cosmetics Directive requires that

Substance	Sodium fluoride	INCI-name
CAS #	7681-49-4	CAS = Chemical Abstracts Service
EC #	231-667-8	EC = European Community Number
Name of Common Ingredients Glossary		
INN/ISO/AN		
Regulation	(EC) No 344/2013	(Admentments to the Cos.-Directive)
Other Directives/Regulations		
Annex/Ref #	III/31	Annex III, position 31, same information as here
Product Type, body parts	Oral products	Toothpastes
Maximum concentration in ready for use preparation	0,15 % calculated as F. When mixed with other fluorine compounds permitted under this Annex, total F concentration must not exceed 0,15 %	
Other		
Wording of conditions of use and warnings	Contains sodium fluoride For any toothpaste with compounds containing fluorine in a concentration of 0.1 to 0.15% calculated as F unless it is already labelled as contra-indicated for children (e.g. "for adult use only"), the following labelling is obligatory: "Children of 6 years and younger: use a pea-sized amount for supervised brushing to minimise swallowing. In case of intake of fluoride from other sources consult a dentist or doctor."	Warning on the label
SCCS opinions Scientific Committee on Consumer Safety provides further notes for use of sodium fluoride for children	• 0653/03 - Opinion concerning the Safety of Fluorine Compounds in Oral Hygiene Products for Children under the Age of 6 years • 0882/05 - Opinion on the Safety of Fluorine Compounds in Oral Hygiene Products for Children under the Age of 6 Years • 1214/09 - Clarification on the Opinions SCCNFP/0653/03 and SCCP/0882/05 on the Safety of Fluorine Compounds in Oral Hygiene Products for Children under the Age of 6 Years	

Figure 1.3 Result of the search in the CosIng database for sodium fluoride.

only a small amount may be taken from the adult toothpaste (see warning in Figure 1.3).

There are numbers for the exact identification of ingredients. The well-known CAS numbers, numerical identifiers of chemical substances, are provided by the Chemical Abstracts Service. Another unique seven-digit identifier for substances is the European Community Number (EC Number), which was determined by the European Commission for regulatory purposes within the European Union. The new EC Number comprises three individual substances characterizing numbers, namely the European Inventory of Existing Commercial Chemical Substances (EINECS), the European List of Notified Chemical Substances (ELINCS), and the No-Longer-Polymers (NLP) list. In detail, these are the lists of the EINECS (over 100 000 entries), the ELINCS (more than 4000 entries), and further the NLP-List (NLP-Number with 700 entries). As shown in Figure 1.3, the two numbers, CAS and EC, are now available in CosIng for precise identification.

In the United States, the search engine of the US Association for the Cosmetic and Personal Care Industry is preferred as database. With more substances and information, the database is probably incomparably in the wealth of information [16]. This Cosmetic Ingredient Dictionary provides a comprehensive listing of ingredients used in cosmetic and personal care products for the benefit of consumers. It is authored by the Personal Care Products

Council, the trade Association for the Cosmetic and Personal Care Industry. The combined dictionary/handbook contains more than 13 000 INCI labeling names for the United States, the European Union, and other countries. These are cross-referenced to nearly 60 000 trade and technical names and 3000 suppliers from 91 countries. The U.S. FDA defined the Cosmetic Ingredient Dictionary as the primary source for ingredient names, which are required for cosmetic ingredient labeling. The benefit is the consistency and transparency provided to consumers and scientists as ingredients are identified by a single labeling name regardless of the national origin of the product. Sodium fluoride is also used as an example. In addition to chemical information, the restrictions in application are shown in Figure 1.4. The FD&C allows less fluoride in toothpastes than the European regulation. In Canada, fluoride-containing dentifrices are prohibited.

[Code of Federal Regulations]
[Title 21, Volume 5]
[Revised as of April 1, 2016]
[CITE: 21CFR355.10]

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER D--DRUGS FOR HUMAN USE

PART 355 -- ANTICARIES DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

Subpart B--Active Ingredients

Sec. 355.10 Anticaries active ingredients.

The active ingredient of the product consists of any of the following when used in the concentration and dosage form established for each ingredient:

(a) ***sodium fluoride*** --(1) *Dentifrices containing 850 to 1,150 ppm theoretical total fluorine in a gel or paste dosage form.* **sodium fluoride** 0.188 to 0.254 percent with an available fluoride ion concentration =650 parts per million (ppm).

(2) *Dentifrices containing 850 to 1,150 ppm theoretical total fluorine in a powdered dosage form.* **sodium fluoride** 0.188 to 0.254 percent with an available fluoride ion concentration of [gteqt]850 ppm for products containing the abrasive sodium bicarbonate and a poured-bulk density of 1.0 to 1.2 grams per milliliter.

(3) *Treatment rinses.* (i) An aqueous solution of acidulated phosphate fluoride derived from **sodium fluoride** acidulated with a mixture of sodium phosphate, monobasic, and phosphoric acid to a level of 0.1 molar phosphate ion and a pH of 3.0 to 4.5 and which yields an effective fluoride ion concentration of 0.02 percent.

(ii) An aqueous solution of acidulated phosphate fluoride derived from **sodium fluoride** acidulated with a mixture of sodium phosphate, dibasic, and phosphoric acid to a pH of 3.5 and which yields an effective fluoride ion concentration of 0.01 percent.

(iii) **sodium fluoride** 0.02 percent aqueous solution with a pH of approximately 7.

(iv) **sodium fluoride** 0.05 percent aqueous solution with a pH of approximately 7.

(v) **sodium fluoride** concentrate containing adequate directions for mixing with water before using to result in a 0.02-percent or 0.05-percent aqueous solution with a pH of approximately 7.

(b) *Sodium monofluorophosphate* --(1) *Dentifrices containing 850 to 1,150 ppm theoretical total fluorine in a gel or paste dosage form.* Sodium monofluorophosphate 0.654 to 0.884 percent with an available fluoride ion concentration (consisting of PO3 F= and F- combined) =800 ppm.

(2) *Dentifrices containing 1,500 ppm theoretical total fluorine in a gel or paste dosage form.* Sodium monofluorophosphate 1.153 percent with an available fluoride ion concentration (consisting of PO3 F= and F- combined) =1,275 ppm.

(c) *Stannous fluoride* --(1) *Dentifrices containing 850 to 1,150 ppm theoretical total fluorine in a gel or paste dosage form.* (i) Stannous fluoride 0.351 to 0.474 percent with an available fluoride ion concentration [gteqt]700 ppm for products containing abrasives other than calcium pyrophosphate.

(ii) Stannous fluoride 0.351 to 0.474 percent with an available fluoride ion concentration [gteqt]290 ppm for products containing the abrasive calcium pyrophosphate.

(2) *Preventive treatment gel.* Stannous fluoride 0.4 percent in an anhydrous glycerin gel, made from anhydrous glycerin and the addition of suitable thickening agents to adjust viscosity.

(3) *Treatment rinse.* Stannous fluoride concentrate marketed in a stable form and containing adequate directions for mixing with water immediately before using to result in a 0.1-percent aqueous solution.

Figure 1.4 Sodium fluoride in the US database . Source: Data from Ref. [16].

Substance	Thioglycolic acid and its salts
CAS #	68-11-1
EC #	200-677-4
Name of Common Ingredients Glossary	THIOGLYCOLIC ACID
INN/ISO/AN	
Regulation	(EC) No 1223/2009
Regulated By	88/233/EEC
Other Directives/Regulations	
Annex/Ref #	III/2a
Product Type, body parts	(a) Hair products (b) Depilatories (c) Hair rinse-off products (d) Products intended for eyelash waving
Maximum concentration in ready for use preparation	(a) 1) 8% 2) 11% (b) 5% (c) 2% (d) 11% The abovementioned percentages are calculated as thioglycollic acid
Other	(a) General use ready for use pH 7 to 9.5 Professional use ready for use pH 7 to 9.5 (b) ready for use pH 7 to 12.7 (c) ready for use pH 7 to 9.5 (d) ready for use pH 7 to 9,5
Wording of conditions of use and warnings	Condition of use: (a) (b) (c) Avoid contact with eyes In the event of contact with eyes, rinse immediately with plenty of water and seek medical advice (a) (c) (d) Wear suitable gloves Warnings to be printed on the label: (a) (b) (c) Contains thioglycolate Follow the instructions Keep out of reach of children (a) (d) For professional use only: Cotains thiglycolata, folow the instruction.
SCCS opinions	• 1520/13 - Thioglycolic acid and its salts (TGA)
Chemical/IUPAC Name	
Identified INGREDIENTS or substances e.g.	• AMMONIUM THIOGLYCOLATE • CALCIUM THIOGLYCOLATE • CALCIUM THIOGLYCOLATE HYDROXIDE • ETHANOLAMINE THIOGLYCOLATE • MAGNESIUM THIOGLYCOLATE • POTASSIUM THIOGLYCOLATE • SODIUM THIOGLYCOLATE • STRONTIUM THIOGLYCOLATE • THIOGLYCOLIC ACID

Figure 1.5 Results of the search in the CosIng database for "thioglycolic acid and its salts."

As a second example for testing the CosIng database, a chemical substance was selected, which cleaves amide and disulfide bonds. As the cream is applied to hairy areas, the substance acts as a hair-removing agent. The salts of thioglycolic acid, such as potassium thioglycolate, are suitable for cleavage. When searching for "potassium thioglyconate" in the CosIng database (CAS # 34452-51-2, EC # 252-038-4), a reference is made to the Annexes of the Cosmetics Regulation. "Thioglycolic acid and its salts" are found there. Unfortunately, the warnings are missing in the current issue. Therefore, under "thioglycolic acid," a new search in CosIng has to take place, which leads to the goal, if all hints are observed.

Figure 1.5 shows the result of the search. There the maximum permissible amount and the permitted pH range are specified for hair removal (depilation). Furthermore, CosIng disclosed the prescribed wording for the warnings. In this exceptional case, CosIng offers more and more detailed information than the Annexes of the Cosmetics Regulation. It also shows that an intensive search for restricted use substances can be necessary. In addition, there is a reference to the detailed opinion of the Scientific Committee on Consumer Safety (SCCS) on the use of this substance group. Safety instructions for pure potassium thioglyconate in aqueous solution are given in the safety data sheet (SDS) of the manufacturer (example: Bruno Bock). For the removal of the hair, precise instructions for the application and the maximum duration of use are required because the formulations are strongly alkaline (warning: contains alkali). Good formulations contain substances, such as weak acids and a buffer, to correct the strongly alkaline pH as well as skin-protecting and skin-soothing substances, which altogether help to reduce the negative effects of the alkali.

1.8 Regulations in the United States

In the United States, the FDA is the competent regulatory authority, a department of Health and Human Services [17]. The top priority of FDA is the protection of consumers. Within the FDA, the cosmetics are integrated in the Center for Food Safety and Applied Nutrition (CFSAN), which is responsible for regulation and approval of food for human consumption, such as food additives, color additives, and cosmetics. Within the authority, cosmetics are the least regulated products. Sunscreens are subject to the Medicine Act in the United States. The problem is discussed in Section 7.16.4.

The US Federal Food, Drug, and Cosmetic Act (abbreviated as FDCA, or FD&C) is a set of laws passed by Congress in 1938. For cosmetics, the laws are amended in title 21 of the United States Code (21 U.S.C.), Chapter 9. They authorize the FDA to oversee the safety of food, drugs, and cosmetics. For cosmetic products, the Act prohibits the marketing of unsafe or mislabeled cosmetics. Therefore, the FDA does not approve cosmetic products but remove cosmetics from the market that contain unsafe ingredients or are mislabeled. A regulation as in Europe does not exist. The mostly unwritten rules are similar to the European ones, for example, what information must be on the packaging. An examination is only carried out if a violation of the written regulations is

found. Then, the FDA imposes high penalties. The FDA can inspect cosmetics manufacturing facilities to ensure quality. The manufacturer of cosmetics is obliged to comply with the regulations. Above all, he must ensure the safety and stability of the products as well as make truthful statements about the product on the packaging.

1.9 Regulations of the Cosmetics Markets in Asia

The ASEAN Cosmetic Directive (ACD, [18]) was created to eliminate restrictions for the trading of cosmetic products among Member States through adoption and implementation of harmonized technical requirements. The Directive represents in large parts a reproduction of the EC Regulation and was signed 2 September 2003 in Cambodia by the Economic Ministers. Since 1 January 2008, the ACD has entered into force in ASEAN Member States after transposing into local regulations. The ACD contains the following subjects, comparable with the European Cosmetics Regulation:

1. General Provisions
2. Definition and Scope
3. Safety Requirements
4. Ingredient Listings
5. ASEAN Handbook of Cosmetic Ingredients
6. Labeling Requirements
7. Product Claims
8. Product Information
9. Methods of Analysis
10. Institutional Arrangements
11. Special Cases
12. Implementation

The Member States (Indonesia, Thailand, Vietnam, China, Japan, Hong Kong, India, Korea, Taiwan, and Philippines) implemented the ACD principles, followed by other states (Brunei Darussalam, Cambodia, Laos, Malaysia, and Singapore). The main principles are as follows:

- Product notification;
- P.I.F. requirement;
- Annexes to control ingredients;
- GMP–GDP (good distribution practice) requirements; and
- Postmarket surveillance.

Annexes II–VI of the prohibited and restricted substances as well as the permitted dyes, preservatives, and UV filters also comply with European requirements [18, 19]. The company or person responsible for marketing the cosmetic products shall ensure that the product will not cause damage to human health when applied under normal or reasonably foreseeable conditions of use. This is actually a matter of course. Before marketing, the product formulation has to be notified

to the regulatory authority. Product information and the safety assessment (P.I.F.) must be readily accessible to the regulatory authority. GMP-standard for the manufacture and GDP for the distribution are mandatory. The company should have experience with the legal requirements for cosmetics. Except Thailand, all countries have transposed the ACD into local regulations, with small deviations.

The implementation of the ACD is accompanied by various committees [20], namely the

- *ACC*: The ASEAN Cosmetic Committee coordinated and monitored the implementation of the Directive. ASEAN Secretariat and ASEAN Cosmetic Association (ACA) are composed by representatives of each member state.
- *ACSB*: The task of the ASEAN Cosmetic Scientific Body is to elaborate recommendations for the ACC on safety, technical, and scientific matters.
- *ACTLC*: The ASEAN Cosmetic Testing Laboratory Committee was established as a postmarket surveillance initiative to support the implementation of ACD through establishing and maintaining an efficient quality assurance system in line with international practices and guidelines.

Deviations from the ACD text should be briefly addressed in the case of China and Japan. China's authorities define normal and special cosmetics. Special cosmetics cover the following product categories:

- Sunscreen
- Spot corrector/antipigmentation/whitening
- Slimming
- Breast care
- Hair growth
- Hair colors
- Perms
- Deodorant
- Depilatories

For all imported products and China's special cosmetics, a full dossier and samples have to be submitted to the CFDA (China Food and Drug Administration) for an evaluation by the technical review expert committee. CFDA test them for unauthorized features, toxicology, and sometimes efficacy (sunscreen). The test period for imported specials lasts up to 12 months.

The Japanese Government regulates the cosmetics market through the Ministry of Health, Labor and Welfare according to the Pharmaceutical Affairs Law [21]. Japan published a list of prohibited and restricted ingredients, as well as a positive list of UV filters and preservatives [19]. In Japan, the cosmetics market is divided into cosmetics and quasi-drugs. Products against acne and dandruff or skin chapping as well as for whitening (bleaching) or sterilizing the skin are among the quasi-drugs, furthermore, products for prevention of foul breath or body odor, promotion of hair growth, or removal of hair, hair dyes, and waving of hair. All these quasi drugs need a special, time-consuming registration. After notification, the other cosmetics with ingredients of the positive list can be easily marketed.

1.10 Delimitation of Cosmetic Products

The delimitation of cosmetics from neighboring areas (Figure 1.6) is not uniformly regulated around the world. Therefore, it is necessary to check for each country whether the product group is classified as cosmetics. These delimitations also play a role in the determination of market sizes in the individual countries. In some cases, unfortunately, it is not clear whether certain products are cosmetics or not, this concerns, for example, sunscreens, depilatories or hygienic articles, and many others. Therefore, the published statistics provide partly very different values (Chapter 2).

Products, which do not belong to cosmetics, are subject to other legal regulations. For some cosmetics-related articles, there is another law (LFGB [6]) in Germany. Objects intended to come into contact with the mucous membranes of the mouth as well as objects intended for personal care fall under the LFGB (§ 5, Nos. 3 and 4). This is why in Germany, the toothbrushes belong to the items of daily necessities and not to cosmetics, in contrast to other European Countries. The same applies to nail files, scissors, razor blades and shavers, combs and hairpins, as well as sponges, towels, and washcloths. In most countries, oral hygiene products (toothpaste, toothbrushes, and the like) are considered to be cosmetics, although they correspond to the definition of medical devices. The hygienic articles, which could be assigned to cosmetics, include, for example, the cotton swabs, tissues, and baby diapers but belong to the items of daily necessities and are subject to the relevant law.

The Medical Device Directive (MDD), also called Directive 93/42/EEC [22], regulates the safety and medical–technical performance of medical devices in the European Economic Area together with Directives 90/385/EEC and 98/79/EC. The amending to the Directives became legally binding in the EU on 21 March 2010 in the directive 2007/47/EC [23]. All apparatus, instruments, and aids used for the medical care of humans by the physician are called medical devices, as well

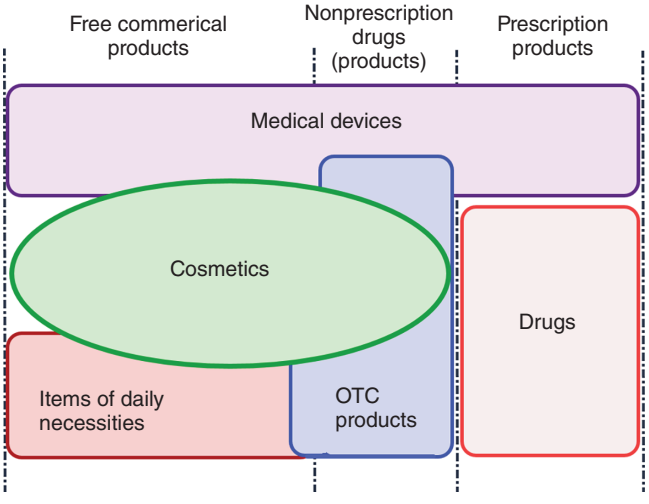


Figure 1.6 Overlaps of the cosmetics with neighboring areas.

Figure 1.7 Medical products characterized by the prescribed CE symbol: (a) sterile liquid for moistening the eyes in a dispenser for dosing individual drops (OTC), (b) rinsing and storage solution for contact lenses, (c) adhesive cream for dentures, and (d) blood pressure gauge with cuff, the CE mark is on the back.

as all the aids and tools that patients need. On the one hand, the devices enhance or save lives and support healing processes; on the other hand, people need different medical devices (products) to improve their lives. Especially, they are objects or substances, used for hygienic care and medical or diagnostic purposes, and which are generally physically or physically chemically active.

In Europe, medical devices must bear the CE marking before they may be placed on the market or put into service. The CE marking presupposes that the products meet the requirements and that this is confirmed by the prescribed conformity assessment (Figure 1.7). Some concrete examples of the devices, assigned to four classes (I, IIa, IIb, and III), are bandages, medical plasters, support stockings, wheelchairs, disinfectants (for equipment), one-way injection, hearing aids, dental materials, dentures, contact lenses, glasses, respirators and dialysis machines, heart catheters, and breast implant. Not only the contact lenses belong to the medical products but also the cleaning liquid and the storage solution, as well as the denture adhesive cream and special cleansers. In contrast, the toothpaste used for the cleaning of dentures belongs to cosmetics. The category of medical products also comprises the physical contraceptives. According to EU Directive 93/42/EEC, sucking incontinence aids are medical devices/class I, like incontinence pants (in contrast to diapers, assigned to the items of daily necessities). A number of products that can be bought in drug stores or in pharmacies belong to the category of medical devices.

If, because of their ingredients, a product restores, corrects, or modifies physiological functions by exerting a pharmacological, immunological, or metabolic action, the product shall be qualified as a drug (medicinal product or therapeutic agent). However, products that, while having an effect on the human body, do not significantly affect the metabolism and thus do not strictly modify the way in which it functions may be qualified as cosmetic products. The FD&C Act defines drugs, in part, by their intended use, as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" and "articles (other than food) intended to affect the structure or any function of the body of man or other

animals." In the Directive 2001/83/EC [24] of the European Parliament and of the Council of 6 November 2001, the following definition can be found (Article 1, § 2):

> Medicinal product:
>
> (a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or
> (b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action or to making a medical diagnosis.

Claims stated on the product labeling that descript medical effects are forbidden for cosmetics. Examples for forbidden claims are restore hair growth, reduce cellulite, treat varicose veins, increase or decrease the production of melanin (pigment) in the skin, or regenerate cells.

According to the FA&C Act, a product can be a drug, a cosmetic, or a combination of both [8]. There are products that meet the definitions of both cosmetics and drugs. Examples display Table 1.5. Depending on the country,

Table 1.5 Product examples with allocation to cosmetics or OTC or drugs.

Product/substance	Cosmetic function	Medical function
Anti-dandruff shampoo	Shampooing	Anti-dandruff agent, e.g. Piroctone Olamine
Fluoride-containing toothpaste	Cleaning the teeth, restoration of oral hygiene	Harden the enamel by sodium fluoride or tin fluoride
Deodorant/ antiperspirant	Prevention of sweat decomposition, binding of smell, perfuming	Inhibiting of sweat production, aluminum compounds
Hair growth liquid or spray	Hair and scalp care	Hair growth stimulating substance, biotin, peptides, hormones
Sunscreen cream, foundations	Skin care	UVA and UVB blocker, see Annexes of the Cosmetic Directive
Anti-acne	Low-fat cleansing cream	Anti-inflammatory, disinfectant, keratolytic substances such as allantoin, salicylic acid, and chlorhexidine, benzoyl peroxide
Hormone cream	Skin care	Hormone such as estrogens, phytohormones with estrogen-like effect
Fragrance	Promoting attractiveness	Aromatherapy, support for falling asleep
Dexpanthenol	"Beauty vitamin"	Healing wounds
Jasmine oil	Enchanting fragrance	Relaxation (previously administered to facilitate births)
Evening primrose oil	Skin care	Agent against atopic dermatitis

the product will be assigned and must fulfill both laws in some countries. Based on the superordinate regulations, the regulatory authority of each country determines in disputed questions the allocation of cosmetic and OTC products (over-the-counter). In other cases, the classification also takes place according to the intended use and the claim on the packaging. As the manufacturer wants, special products can be marketed both as cosmetics or medicament. Therefore, the product of Figure 1.1 with the labeling "support the self-healing processes of the skin" is only an effective cosmetic product, although it can smooth neurodermitic skin. Such products are referred to in the literature as "cosmeceuticals," although this term does not appear in laws. If, on the other hand, the mentioned product is advertised with the claim "cream for removing scaly, neurodermitic skin," it would be an OTC product. It is clear that they have to fulfill the corresponding law. These statements also include some products that are called "quasi drugs" in Japan or "special cosmetics" in China.

The description "OTC" is referred to nonprescription medicines, which are preferably sold through the pharmacy [25]. In cases of low, typical symptoms, people perform a self-medication with OTC medicines. The OTC area comprises different product groups depending on the country. Figure 1.8 gives some examples. According to Article 48 of the German Medicines Act, the Federal Ministry of Health classifies medicinal products as nonprescription if they, based on the formulation and experience, cannot endanger the user's health, even without medical supervision. The condition is that they are used as intended. An expert committee develops proposals, whose substances can be released from the prescription obligation or must be subordinated to it.

Figure 1.8 Much purchased OTC products: (a) wound and healing ointment, (b) pain gel, (c) headache tablet, and (d) cough syrup.

Figure 1.9 Typical drugs: (a) cortisone-containing skin ointment, (b) antibiotic, (c) tablets for blood pressure regulation, and (d) statins for cholesterol lowering.

The manufacturer can optionally change a cosmetic product into an OTC article by complying with the requirements of a drug and allowing only a sale through the pharmacies. Through this way of marketing, L'Oréal goes successfully with the "active cosmetics" series, which also includes the known Vichy skin creams.

The doctor can prescribe medicines for the whole body and for all organs. Some examples of skin, heart, and vein problems as well as bacterial infections can be found in Figure 1.9. In contrast to cosmetics, the drugs act preferably inside the body that means systemic.

1.11 Learnings

- ✓ In Europe, the Cosmetics Regulation (EC) No 1223/2009 clarifies what cosmetic products are and prescribes the ingredients in type and quantity, manufacture and marketing, as well as the responsibilities of the manufacturer.
- ✓ There are very similar regulations in Asia. In the United States, the regulations are not so comprehensive and less stringent.
- ✓ The marketer is responsible for his product worldwide and ensures that all steps, from the formulation to the consumption, follow the guideline.
- ✓ Each manufacturer must provide a P.I.F. for each product/product group that includes the product description and in particular a detailed safety assessment by an expert.
- ✓ The Cosmetics Regulation requires the product to be registered with the competent authority. In Europe, formulations must be submitted electronically to the CPNP.
- ✓ The regulation contains in the Annexes the permissible ingredients, including the colors, preservatives and UV filters, and specifies permissible limits. The restrictions of ingredients can be easily found in the CosIng (**Cos**metic **Ing**redients) database.
- ✓ The manufacturer should usefully protect its brand name in the Patent and Trademark Office.
- ✓ Cosmetic products should be distinguished from items of daily use as well as medical devices and OTC products for which other laws apply.

References

1 Stepanovs, J. (1999). *Skin Saver Remedies*. Australia: Harald W. Tietze Publishing.

2 Umbach, W. (ed.) (2004). *Kosmetik und Hygiene: von Kopf bis Fuß*, 3e. Weinheim: Wiley-VCH.

3 History of cosmetics, from Wikipedia, the free encyclopedia, 2019 https://en.wikipedia.org/wiki/History_of_cosmetics (accessed 6 May 2019).

4 Stewart, S. (2017). *Painted Faces: A Colourful History of Cosmetics*. Amberley Publishing.

5 REGULATION (EC) No 1223/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 30 November 2009 on cosmetic products. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:342:0059:0209:EN:PDF (accessed 17 November 2018). http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:342:0059:0209:DE:PDF (accessed 17 November 2018)

6 Lebensmittel-, Bedarfsgegenstände- und Futtermittelgesetzbuch (Lebensmittel- und Futtermittelgesetzbuch - LFGB), 2005. http://www.gesetze-im-internet.de/lfgb (accessed 17 November 2018).

7 Kirk-Othmer (2013). *Kirk-Othmer Chemical Technology of Cosmetics*. Hoboken, NJ: Wiley.
8 U.S. Food & Drug Administration, Is it a cosmetic, a drug, or both?. https://www.fda.gov/Cosmetics/GuidanceRegulation/LawsRegulations/ucm074201.htm (accessed 17 November 2018).
9 Verordnung über kosmetische Mittel (Kosmetik-Verordnung), KosmetikV 2014. https://www.gesetze-im-internet.de/bundesrecht/kosmetikv_2014/gesamt.pdf (accessed 17 November 2018).
10 Gesetz über die Werbung auf dem Gebiet des Heilwesens (Heilmittelwerbegesetz - HWG), 1965. https://www.gesetze-im-internet.de/heilmwerbg/BJNR006049965.html (accessed 17 November 2018).
11 DPMAregister, Beginner's search, 2019. https://register.dpma.de/DPMAregister/marke/einsteiger?lang=en (accessed 6 May 2019).
12 EUIPO, European Union Intellectual Property Office, 2019. https://euipo.europa.eu/ohimportal/en/trade-marks-in-the-european-union (accessed 6 May 2019).
13 Directive 2008/95/EC of the European Parliament and of the Council, 22 October 2008, to approximate the laws of the Member States relating to trade marks. http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32008L0095 (accessed 17 November 2018).
14 European Commission, Cosmetic Product Notification Portal (CPNP). https://ec.europa.eu/growth/sectors/cosmetics/cpnp_en (accessed 17 November 2018).
15 European Commission, Cosmetic ingredient database (Cosing). https://ec.europa.eu/growth/sectors/cosmetics/cosing_en (accessed 17 November 2018).
16 Cosmetics Info, Cosmetic Ingredient Dictionary, 2016. http://www.cosmeticsinfo.org/Ingredient-dictionary (accessed 17 November 2018).
17 U.S. Food & Drug Administration, Cosmetics, https://www.fda.gov/Cosmetics/default.htm (accessed 17 November 2018).
18 Health Sciences Authority (HSA), ASEAN Cosmetic Directive, 2017. https://www.hsa.gov.sg/content/hsa/en/Health_Products_Regulation/Cosmetic_Products/Overview/ASEAN_Cosmetic_Directive.html (accessed 17 November 2018).
19 Standards for Cosmetics (Ministry of Health and Welfare Notification No.331 of 2000), Japan. http://www.mhlw.go.jp/file/06-Seisakujouhou-11120000-Iyakushokuhinkyoku/0000032704.pdf (accessed 17 November 2018).
20 Asean Cosmetics Association, ASEAN Cosmetic Directive, 2019. http://aseancosmetics.org/information-center/asean-cosmetic-directive/(accessed 18 November 2018).
21 Information on Japanese Regulatory Affairs Regulatory Information Task Force Japan Pharmaceutical Manufacturers Association, 2015. http://www.jpma.or.jp/english/parj/pdf/2015.pdf (accessed 18 November 2018).
22 COUNCIL DIRECTIVE 93/42/EEC of 14 June 1993 concerning medical devices. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1993L0042:20071011:en:PDF (accessed 18 November 2018).
23 DIRECTIVE 2007/47/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 September 2007 amending Council Directive

90/385/EEC on the approximation of the laws of the Member States relating to active implantable medical devices, Council Directive 93/42/EEC concerning medical devices and Directive 98/8/EC concerning the placing of biocidal products on the market. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:247:0021:0055:en:PDF (accessed 18 November 2018).

24 DIRECTIVE 2001/83/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 6 November 2001 on the Community code relating to medicinal products for human use. http://ec.europa.eu/health//sites/health/files/files/eudralex/vol-1/dir_2001_83_consol_2012/dir_2001_83_cons_2012_en.pdf (accessed 18 November 2018).

25 Over-the-counter drug, From Wikipedia, the free encyclopedia, 2019. https://en.wikipedia.org/wiki/Over-the-counter_drug (accessed 6 May 2019).