The Modernization of the US Cosmetic Regulation Act of 2022:

An Overview of the New Challenges for Small and Medium Enterprises in the USA

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Kathleen Grundke

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Betreuer und Erstgutachter: Dr. J. Hofer

Zweitgutachterin: PD Dr. A. Schiedel

Table of Contents

List of Abbreviations

AE	Adverse Event
CFR	Code of Federal Regulations
CPNP	Cosmetic Product Notification Portal
CPSR	Cosmetic Product Safety Report
EC	European Commission
EMA	European Medicines Agency
FDA	U.S. Food and Drug Administration
FD&C Act	Food, Drug & Cosmetics Act
FTC	Federal Trade Commission
GMP	Good Manufacturing Practices
ICH	International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
INCI	International Nomenclature of Cosmetic Ingredients
ISO	International Organization for Standardization
MoCRA	FD&C Act amended under Modernization of Cosmetics Regulation Act of 2022
MS	Member State
RP	Responsible Person
SAE	Serious Adverse Event
SAER	Serious Adverse Event Report
SME	Small and Medium Enterprises
SUE	Serious Undesirable Effect
PIF	Product Information File
PV	Pharmacovigilance
VCRP	Voluntary Cosmetic Registration Program

List of Figures

List of Tables

1. Introduction

Cosmetic products have a long history, with evidence of their use dating back to ancient civilizations. In ancient Egypt, both women and men used scented oils and kohl to cleanse and enhance their appearance (1–3).Figure 1 shows an Egyptian queen as a painted limestone statue wearing kohl as eye make-up.

Figure 1: Hatshepsut, an Egyptian queen, is depicted on a painted limestone statue in the Egyptian Museum in Cairo. Source: https://www.nationalgeographic.com/science/article/100114-cleopatra-eye-makeup-ancient-egyptians (4)

In addition to its aesthetic use, kohl served hygienic, therapeutic, and religious purposes, it was believed to protect eyes from infections and used to treat eye irritations. In ancient Egypt, it often contained lead, which was posing health risks over time, though these risks were unknown then (3, 4).

In the 16th century, lead powder was used to achieve pale and smooth skin. One particularly well-known user was Queen Elizabeth I. The queen used "*Spirits of Saturn*", a mixture of lead and vinegar, which led to pale skin, but in the long run caused teeth decay and hair loss(5). In the 19th century, cosmetic products containing lead and arsenic were recognized as dangerous, but the usage continued into the 20th century. Cosmetics were initially for the upper classes but became widely available during industrialization. In the early 20th century, arsenic wafers became popular in the USA, despite their harmful effects (6). Figure 2 illustrates an advertisement for "*Ammet's French complexion wafers*" claiming facial imperfections are permanently removed, leaving a clear complexion and smoother features, while being completely safe to use.

Figure 2: Advertisement of Ammet's French Complexion Wafers of 1890. Source: https://www.cosmeticsandskin.com/ded/arsenic.php (7)

The recognition of the harmfulness of some cosmetic products gradually led to changes in the cosmetic section and a growing awareness of the need for safe ingredients. Over time, cosmetic products have evolved and are now an integral part of daily routines. Today, a wide range of cosmetic products is used for various purposes, e.g. baby products such as shampoo or eye make-up preparation as eyebrow pencil (8, 9).

In the past numerous incidents caused by unsafe products have resulted in serious health problems in the United States of America (USA) as well as European Union (EU) that has shown the need for stricter regulatory requirements in the cosmetic sector (10, 11).

The cosmetic market in the USA is a rapidly growing, generating approximately $66.74 billion in sales in 2024 (12). In comparison, the EU market comprises estimated $131.66 billion in 2024 and also represents an important and high potential sales market (13). Due to the EU's low import duties as the EU does not impose customs duty on some cosmetic products, e.g. hair products, lip and eye make-up, the European cosmetics sector is attractive for small and medium-sized (SME) US exporters (14).

The history of the cosmetic EU regulation began in 1976 and is therefore more recent than cosmetics regulation in the USA. In 2009, the Council Directive 76/768/EEC was replaced by EU Regulation No. 1223/2009. It formed a more strictly regulated framework, particularly regarding requirements for manufacturing and marketing of cosmetic products. In contrast

to the US regulation which places more emphasis on individual responsibility of a company for the safety of its cosmetic products (15, 10).

In the USA, cosmetic product safety was gradually improved through legislation, especially after incidents like the harmful eyelash dye “Lash Lure.” Key regulations include the Federal Food, Drug, and Cosmetic Act (FD&C Act) of 1938, which was later expanded by the Fair Packaging and Labeling Act of 1966 and the Modernization of Cosmetics Regulation Act (MoCRA) in 2022. As a consequence of the implementation of MoCRA, the Federal Drug Administration (FDA) terminates the Voluntary Cosmetic Registration Program (VCRP), the only program available for companies to voluntarily register cosmetic products until then (16)

The FD&C Act under MoCRA increased FDA authority and introduced new requirements that may affect especially SMEs, which are vital to the economy. SMEs play a crucial role, accounting for two-thirds of jobs in the US and 99% of businesses in the EU, driving innovation and economic growth (17–19).

2. Aim of this Thesis

The aim of this thesis is to analyze the new challenges faced by cosmetic companies, particularly SMEs, due to the updated cosmetics regulation in the USA following the enactment of MoCRA. The focus will be on the specific requirements and regulations for cosmetics under MoCRA, along with a comparison to the corresponding provisions of the EU Cosmetics Regulation. Additionally, the most significant parallels and differences with the respective pharmaceutical legislation in the USA and the EU will be examined.

A case study will be presented. It will focus on a US-based SME that meets the definition of small business and sells several cosmetic products with an annual turnover of $750,000 in the USA, will be used to investigate the practical implications of the changes mandated under MoCRA. The aim is to detail the challenges and burdens faced by SMEs and to assess whether a unified registration strategy for a cosmetic product for the USA and Europe can be developed to adapt to the new conditions.

The analysis aims to develop practical recommendations tailored specifically to the needs of SMEs, supporting them in strategic decision-making and adaptation to the expansion of FDA's authority to regulate cosmetics.

3. Regulatory Framework of Cosmetic Products in the USA

3.1. History of Cosmetics Products under FDA's Regulation

This section provides an overview of the historical development of cosmetics legislation. It outlines the development of the legal framework from its beginnings to the current standards and highlights the most important milestones that have affected the safety and market surveillance of cosmetic products. The implementation of the FD&C Act of 1938 was the first step towards the regulation of food, drug and cosmetics as shown in Figure 3.

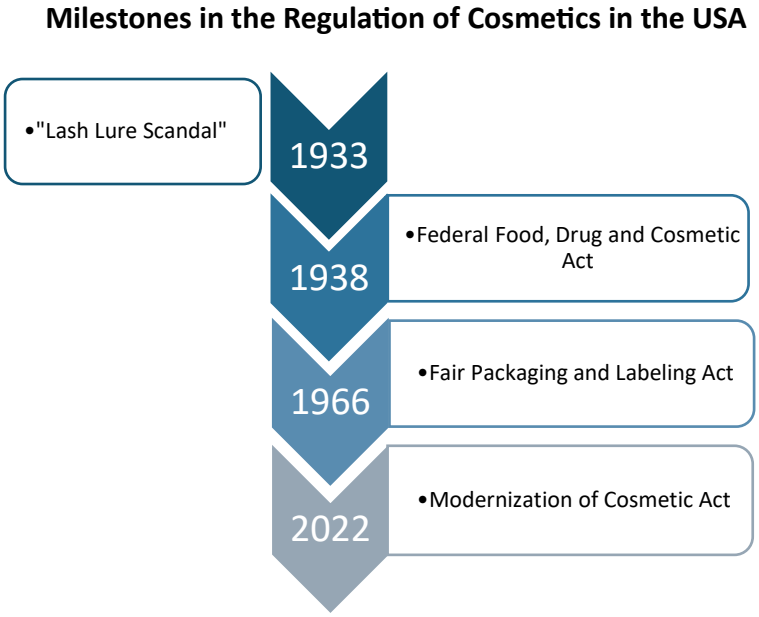

Figure 3: The image represents the most important milestones in the regulation of cosmetic products in the USA.

The FD&C Act, was extended to include cosmetic products and medical devices in response to growing safety concerns (20, 10) (Figure 3). One example of a safety concern was the infamous case of "*Lash Lure*" in 1933, a coal tar-based eyelash dye that caused severe eye injuries, including blindness, and at least one fatality (21). Figure 4 shows a poster established from the FDA to warn consumers of "Lash Lure" from the consequences of use.

Figure 4: Close-up of the FDA ad in which the dangers of Lash Lure are emphasized, with before and after photos of the woman who went blind after using Lash Lure. (Image source: https://www.cosmeticsandskin.com/bcb/lash-lure.php) (22)

Among others, this case has led the FDA to impose stricter requirements on the use of color additives. In response to concerns about the safety of colorants and their potential impact on consumer health the FDA demands under the FD&C Act, starting 1938, color additives must be approved by the FDA before they can be used in food, drugs and cosmetics. Batch certification is required for colorants made from coal tar. The color certification program, which is funded by user fees, continues to this day (20, 23).

The FD&C Act of 1938 grant the FDA authority to regulate adulterated or misbranded products and ban harmful substances not only in drugs, but also in cosmetics. It requires that cosmetic products are safe for their intended use and properly labeled. However, the FD&C Act did not enforce pre-market safety testing for substances, leaving companies responsible for ensuring the safety of cosmetic products (10, 24).

Because the first definition of proper labeling was very broad, the Fair Packaging and Labeling Act (FPLA) of 1966 refined it to further enhanced consumer protection by requiring that all products marketed to retail consumers, including cosmetics, have to be honestly and informatively labeled. This regulation ensured greater transparency by mandating ingredient lists and standardized labeling, enabling consumers to make informed choices (20, 25).

Apart from legislation, in 1972, the VCRP, a voluntary registration program was founded to provide the FDA with the most accurate estimate of available information on cosmetic products and their ingredients, their rate of usage and the companies involved in their

manufacturing and distribution. The VCRP was also open to foreign cosmetics companies whose products were imported for sale in the USA. The participation in this program was voluntary, it resulted in an incomplete overview of cosmetic products available on the USA market.

The FD&C Act of 1938 remained the basis of cosmetics regulation and was last amended under MoCRA in 2022, which is the most substantial expansion of the FDA's authority to regulate cosmetics since the implementation of the FD&C Act and aims to enhance the cosmetic products' safety that are used by many users every day (9).

The most important legislative changes resulting from the implementation of MoCRA include the obligation for maintaining documentation of safety substantiation, adverse event reporting and the compliance with Good Manufacturing Practices (GMP). In addition, the labeling requirements have been extended, as the detailed contact details of the responsible person (RP) and all fragrances allergens must be listed in detail (9, 26).

Furthermore, under MoCRA the FDA announced to stop accepting submissions to the VCRP on March 27, 2023 as the registration and listing of cosmetic products are now mandatory (27).

The overview of the historical development of cosmetics legislation, starting with the FD&C Act of 1938, which was the first regulation for cosmetic products in the USA, and describes the key milestones that impacted the safety and market surveillance of cosmetic products. The MoCRA of 2022 brought significant expansions of the FDA's authority to regulate cosmetics. The following section 3.2 offers an overview of the current federal regulation of cosmetic products and the changes to the FD&C Act brought about by the implementation of MoCRA.

3.2. Overview of the Federal Regulation of Cosmetic Products in the USA

Two agencies are responsible for enforcing cosmetics regulations. The FDA is responsible for monitoring product safety, responding to consumer complaints, conducting inspections and issuing warning letter or recalls for non-compliant cosmetic products (28). On the other

hand the Federal Trade Commission (FTC) is playing an important role in regulating advertising claims to prevent misleading marketing practices (29). In general, a claim is a statement about the advertised medicine or what it does. Claims usually relate to benefits and can be made directly through a statement or indirectly using images or other graphics. For example, an ad with a picture of Aloe Vera may suggest that the advertised cosmetic product contains Aloe Vera (30).

As already mentioned, the FD&C Act provides the main regulatory framework for cosmetic products in the USA. This legislation establishes a variety of obligations for companies, including the responsibility to ensure safety of the cosmetic product (31).

Cosmetic Products are defined under sec.201(i) of the FD&C Act as a product, except soap, ”*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*..” (32). As a part of the implementation of the MoCRA, the definition of cosmetic products has been extended to *“a preparation of cosmetic ingredients with a qualitatively and quantitatively set composition for use in a finished product*” (33).

As mentioned before, soap is an exception as FDA defines it as a product consisting primarily of alkali salts of fatty acids formed by the reaction of fats or oils with alkali. These salts must be the primary source of the cleansing action; if synthetic detergents are included, the product is classified as a cosmetic product. In addition, soap must be marketed exclusively as a cleaning product which is regulated by the Consumer Product Safety Commission. In contrast, products with additional purposes, such as moisturizing, fragrance or medicinal benefits, are classified as cosmetics or drugs (34). At this point, it must be emphasized once again that it is important to make a clear distinction between cosmetics, drugs and medical devices as each category follows different regulatory pathways (35, 36). For a brief overview of the requirements for drugs please read through section 3.6.

The FD&C Act is supplemented by the Fair Packaging and Labeling Act (FPLA). In general, labeling refers to all labels and other written, printed or graphic information on or accompanying a product and must appear on both inside and outside of the container or packaging. The labeling requirement are laid down in the 21 CFR and all cosmetic products

containing false or misleading statements on the label or are not labeled in accordance with these requirements may be considered adulterated or misbranded and will be susceptible to regulatory measurements, e.g., inspection of establishments or prohibition of distribution (24).

The FPLA requires a clear and accurate product labeling, ensuring that consumers receive important information about the ingredients and its usage (37, 24). In the USA, the label and labelling are closely linked to the advertisement and promotional material. Therefore, the meaning of labeling is only briefly discussed here. Due to its significant importance, a detailed description of the requirements of packaging, label and advertisement is shown (see section 3.3.5.).

Beyond that, the formulation of cosmetic products is an essential part in ensuring their safety and compliance with regulations. This aspect will be examined in more detail in section 3.3.2., where its importance and the factors influencing the development of cosmetic formulations will be discussed.

Under MoCRA, the most important changes are the maintaining documents of the safety substantiation, establishment of cosmeticovigilance system for adverse event reporting and compliance with GMP.

The RP plays a crucial role in ensuring the safety of the cosmetic product (see section 3.3.1 for main responsibilities and functions of the RP). Its responsibility includes the safety substantiation of a cosmetic product, proven by scientifically validated methods and records, where animal testing is not mandatory. Talc-containing cosmetic products require additional testing under MoCRA, which focuses on safety concerns, particularly asbestos contamination and health risks (38) (see section 3.3.3.).

As mentioned before, under MoCRA, compliance with GMP is required in the manufacture of cosmetic products. Nevertheless, the scope of the compliance with GMP is still under review by the FDA (see section 3.3.4. for a detailed description of the GMP requirement).

Furthermore, the labeling requirements have been expanded under MoCRA, especially with regard to mentioning the detailed contact information of the RP and declaration of fragrances, essential to provide both transparency and consumer safety (see section 3.3.5).

The FDA demands the mandatory registration of facilities and listing of cosmetic products with Cosmetics Direct System (see section 3.4)

Beyond that, the adverse event (AE) reporting for cosmetic products to the FDA is now mandatory. Under MoCRA, the RP must report any serious adverse event (SAE) in the USA to the FDA (38–40) (see also section 3.5.1).

Under MoCRA, the FDA can request mandatory recalls in case of safety concerns and the FDA has the authority to order a mandatory recall if the RP fails to do so voluntarily (9). (section 3.5.2).

However, there are certain exemptions for compliance with GMP and for the obligation to register. Facilities are not required to register if they meet the criteria for small businesses. Specifically, the legislation exempts RP, owners, and operators of establishments with average annual gross sales for cosmetic products of less than $1,000,000 (adjusted for inflation) in the USA over the past three years (39). Additionally, in accordance with 21 CFR 710.9 the registration obligation is not applicable for all establishments listed in ANNEX I. No exceptions are made for these type of products (“special-use cosmetic products”) listed in ANNEX I , regardless of whether the definition of small business is met based on annual turnover (40).

To sum up, the FDA and FTC regulate cosmetics in the USA, with the FDA ensuring product safety and the FTC overseeing advertising claims. The FD&C Act under MoCRA requires stricter safety measures, GMP compliance, and mandatory reporting of AE, while also detailing labeling and facility registration requirements. Small businesses are exempt from GMP and registration and listing obligations.

3.3. Pre-Market Requirements in the USA

3.3.1. Responsible Person in the USA

As previously mentioned, RP plays a crucial role in ensuring compliance with regulatory requirements in the cosmetics industry. This section provides a detailed overview of the RP's responsibilities within the context of the applicable legislation. A RP must be determined and is defined as *“manufacturer, packer, or distributor of a cosmetic product whose name appears on the label of such cosmetic product*” (41).

The main responsibilities of the RP include several key tasks that are essential to ensure the safety, quality, and compliance of cosmetic products:

- Maintain the documentation of the safety substantiation:
  The RP is responsible to ensure that safety substantiation for the cosmetic product is maintained and accessible for regulatory authorities to review at any time (38). This involves gathering and keeping detailed records that demonstrate the safety of the product when used according to its intended purpose. The RP is responsible for compiling the necessary documentation, which may include ingredient assessments, toxicological profiles, and clinical testing data (see section 3.3.3. for more details).
- Labeling: Another critical responsibility is ensuring that name and contact details of the RP are clearly indicated on the cosmetic product's label (42, 41) (see section 3.3.5).
- AE Reporting: The RP is responsible for reporting any SAE associated with the use of cosmetic products. This includes tracking and documenting consumer complaints, side effects, or any incidents where the product may have caused harm. The RP must ensure that these reports are submitted to the FDA (43). As this is an important part of cosmeticovigilance, it will be discussed in further detail in section 3.5.1.

Overall, The RP ensures compliance by maintaining safety documentation, proper labeling, and reporting SAE.

3.3.2. Product Formulation in the USA

As stated in section 3.2, the formulation of cosmetic products is an essential part in ensuring their safety and compliance with regulations. Moreover, the classification of a product as a cosmetic or drug depends largely on its intended use, ingredients and formulation. As explained in section 3.6, a product may be regulated as a drug if its composition results in properties that extend beyond cosmetic purposes.

In addition, there are important exceptions to the classification of cosmetic products, which can often lead to confusion. One example is the regulation of self-tanning lotions. In general, products that are intended for external application to the skin and do not have

therapeutic or curative purposes are classified as cosmetic products. A self-tanning lotion that only aims to give the skin a tanned color therefore falls into the category of cosmetic products. However, there is one significant exception to this rule: if the self-tanning lotion also contains active ingredients that have been proven to provide a health benefit, for example by protecting against harmful UV rays, it is no longer considered a purely cosmetic product. Such an active ingredient could, for example, be a sun filter or another active agent to protect against UV damage. In this case, the product would fall under the regulation of drugs in the USA, as it is a therapeutic or health-promoting effect, namely protecting the skin from sunburn, skin ageing or even skin cancer. Similarly, a standard shampoo is classified as a cosmetics, whereas an anti-dandruff shampoo with medical claims falls under drug regulation (44–46).

The FDA enforces strict rules on the ingredients used in cosmetic products. A categorized list of substances that are either prohibited or restricted due to safety concerns is shown in ANNEX II.

Certain cosmetic ingredients have raised health concerns, such as coal-tar hair dyes used as color additives and synthetic compounds like per- and polyfluoroalkyl substances (PFAS). PFAS are intentionally used in cosmetics such as lipsticks, eyeshadows, moisturizers, nail polishes, and cleansers to condition and smooth skin and hair, enhance shine, and improve product texture and consistency (47, 48). As PFAS leads to safety concerns they must be mentioned on the cosmetic label. Now there are currently guidelines issued by the FDA. Under MoCRA, the FDA is requested to evaluate the usage of PFAS in cosmetic products, including any risks associated with their use not later than December 2025 (47).

As mentioned before, the FDA regulates color additives in foods, drugs, cosmetics, and medical devices, approving safe additives and uses in the Code of Federal Regulations (CFR). The usage of an unlisted color additive, the incorrect use of a listed color additive, or the use of a color additive that does not meet the specification of purity and identity of the listing regulation may result in a product being adulterated under the provisions of the FD&C Act (49).

Nanomaterials are increasingly used in cosmetic products in the USA, especially in skincare products, to enhance properties such as skin penetration and texture. While the FDA has

not established formal regulatory definitions for "*nanotechnology*", "*nanomaterial*", "*nanoscale*", or other related terms. In addition, nanoparticles are not directly regulated by the FDA. For this reason, cosmetics companies whose products contain nanomaterials are required to thoroughly test their product and ensure that it is adapted to the specific properties of the nanoscale, e.g. as part of the proof of safety substantiation (50).

In summary, the classification of cosmetic products depends on their intended use, ingredients, and formulation, with exceptions for products that offer therapeutic benefits, such as self-tanning lotions or anti-dandruff shampoos. The FDA regulates cosmetic ingredients for safety, including restrictions on substances like PFAS and color additives, while encouraging innovation in areas like nanotechnology, provided safety assessments are adapted accordingly.

3.3.3. Safety Substantiation and Animal Testing in the USA

As indicated in section 3.2 , there was no obligation to maintain documentation as proof of safety substantiation in the past. However, the companies were required to always ensure the safety of their product. Nevertheless, the safety of cosmetic products has become significantly more stringent under MoCRA compared to previous regulations. As mentioned before, the RP is now required to substantiate the safety of cosmetic products through comprehensive and scientifically validated records (51). In this context, the term safe is defined as a product, including all its ingredients, being harmless to the user when used as intended or under typical and normal conditions of use. It is important to note that a cosmetic product will not be deemed harmful solely because it may cause mild and temporary skin irritation in a subset of users (52). To substantiate safety, companies may rely on existing safety data, provided that the data are obtained through scientifically valid and reliable methods. Such methods include the consideration of existing published studies, literature review , database review and studies (9, 51, 38).

However, unlike in the EU, the use of animal testing is permitted in the USA. While animal testing is not a mandatory requirement for cosmetic products, companies are encouraged to use alternative methods wherever possible. This approach aligns with global trends, such as the complete ban on animal testing for cosmetics in the EU. Additionally, products with

higher risks, such as those containing nanomaterials or talc, may be subject to stricter safety assessments (53, 50). Furthermore, MoCRA emphasizes the safety of products containing talc. Asbestos and talc are natural minerals that often occur together in close proximity in the earth. For this reason, talc can potentially be contaminated with asbestos. Talc is used in a variety of ways in cosmetic products and other personal care products, e.g. face or baby powder. For instance, it can be used to absorb moisture and prevent clumping. Since the 1960s, studies have suggested a possible link between the use of talc-containing powder in the genital area and ovarian cancer, but without conclusive evidence or clarity about possible risk factors. In addition, there have also been concerns about possible asbestos contamination of talc since the 1970s. Under MoCRA, the FDA proposed to introduce standardized test methods for the detection and identification of asbestos contaminants in cosmetic products because asbestos is a known carcinogen (when inhaled). The proposed rule mandates that manufacturers test a representative sample from each batch or lot of talc-containing cosmetic products for asbestos using both Polarized Light Microscopy with dispersion staining and Transmission Electron Microscopy combined with Energy Dispersive Spectroscopy and Selected Area Electron Diffraction (54, 55).

To sum up, MoCRA requires companies to substantiate the safety of cosmetic products with scientifically validated records, and stricter assessments are needed for risk products like those with talc or nanomaterials. While animal testing is permitted, alternatives are encouraged.

3.3.4. Good Manufacturing Practices of Cosmetic Products in the USA

As mentioned before, compliance with GMP has so far not been mandatory for cosmetic products in the USA. In the past, the FDA has relied on companies to be compliant with GMP voluntary and based on recommendations laid down in the draft Cosmetic Good Manufacturing Practices Guideline (56, 9).

Under MoCRA, the compliance with GMP for cosmetics is no longer voluntary, except for small businesses. However, there is a requirement under MoCRA for the FDA to propose binding Cosmetic GMP guidelines. Nevertheless, the scope of requirements for cosmetic products is not yet fully known and must be established by the FDA. It could be expected

that the scope and stringency of potential future Cosmetic GMP requirements may vary depending on the size of the facility. Possibly, larger manufacturers with complex supply chains and production processes are more likely to face stricter obligations, while smaller facilities may see scaled-down requirements to account for their limited resources (57, 58). However, this cannot be said with certainty.

The draft guideline "Cosmetic Good Manufacturing Practices" last amended in June 2013 by the FDA, which is currently available, provides guidance on production, quality control and record keeping processes such as:

- Establishing and maintaining clean and hygienic production environments.
- Conducting regular employee training on hygiene and production protocols.
- Ensuring the validation and maintenance of manufacturing equipment.
- Implementing traceability systems for raw materials and finished products.
- Keeping detailed documentation of production processes and quality control measures.

All in all, under MoCRA, compliance with GMP for cosmetic products in the USA is now mandatory, except for small businesses. However, the full requirements and scope of the GMP guidelines still need to be established by the FDA, with larger manufacturers expected to face stricter obligations. However, the implementation of GMP requirements is seen as a key factor in meeting overall safety and quality expectations. Companies are encouraged to adopt GMP Guidelines to increase consumer confidence and align with international best practices (56).

3.3.5. Packaging, Labeling and Advertisement in the USA

As already stated in 3.2, it should be emphasized that the FDA focusses on packaging and labeling which are closely connected to claims and advertisement (30). The FDA prohibits the marketing of cosmetics that are adulterated or misbranded according to sec. §301 of FD&C Act. Here a cosmetic product is regarded as misbranded if the labeling is not correct or information such as net quantity of contents is not correct or the container or its fill is

misleading (59). Moreover, the sec. §602 of the FD&C Act states that a label can be considered misleading not only if a statement is deceptive, but also if a material fact is omitted, which could be significant due to a statement on the label or the potential consequences of the product's recommended use (60). In brief, misbranded or misleading cosmetics are prohibited to be sold on the USA market (61).

The Federal Trade Commission (FTC) Act also applies to the advertisement of cosmetic products. It requires that advertisements are truthful, supported by evidence, and free from unfair or deceptive practices. This ensures that consumers receive accurate information about the product's benefits and use (62).

Under MoCRA, the FDA does not require pre-approval of cosmetic labels before products are marketed, and there is no centralized list of approved claims. However, all labeling claims must be truthful and not misleading. Companies have to avoid claims that could inadvertently categorize the product as a drug, such as "heals skin conditions" or "treats acne" (63).

Moreover, the type and manner of packaging, images and claims packaging can also influence the intended use. It is therefore important to note that an incorrect presentation of the cosmetic product can lead to the classification of a drug product. This could be the case if (advertising) claims are used on the packaging. Certain claims on product labels, in advertisements, on the internet, or in other promotional materials can result in a product being classified as a drug, even if it is marketed as a cosmetic. For instance, claims of a product as a solution for promoting hair growth, reducing cellulite, or treating varicose veins were cited in FDA warning letters (34, 46).

In 2017, the FDA issued a warning letter for several cosmetic products of “B*e Natural Organics, LLC*”. For example, “*Chamomile Balancing Mist*” was advertised as a cosmetic product. However, the company made claims such as “*Chamomile, lemongrass, edelweiss and milk thistle, the ingredients of Chamomile Balancing Mist, soothe irritated skin with anti-inflammatory properties”*. The FDA raised objects to the claim “*Calming and anti-inflammatory*” as it indicates the function of a drug. The FDA requested to review their website, product labels, and other labeling for their products ensuring claims do not lead to violations of the Act (64) .

Another very important point is the consumer's expectations. In 2017, the FDA issued a warning letter for *“Advanced Hyaluronic Acid Antiaging Serum*” with the claim "*Hyaluronic Acid has recently been used to create Hylaform Gel, an FDA Approved injectable material that aestheticians and plastic surgeons predict will replace collagen injections because the risk of reaction is lower (most collagen being of bovine origin) and Hylaform Gel is more effective, and the results last longer than those of collagen injections*." These statements might give the impression of being particularly effective to the consumer (65, 34, 46).

Nevertheless, ingredients can also have an influence on classification, generally known for therapeutic purposes, e.g. fluoride in toothpaste can lead to the classification of a drug. Such claims suggest the intended use of the product, such as the treatment or prevention of disease or the influencing of the structure or functions of the human body. As soon as a product has these properties, it is classified as a drug. In general, claims must be based on valid scientific evidence and should align with the product's intended cosmetic purpose (46, 63).

MoCRA introduces significant changes to the regulation of cosmetic products in the USA, particularly in the area of ingredient transparency and safety, following the model of international regulations like those in the EU (9, 51). One notable change involves the labeling of fragrance allergens. Previously, fragrances did not require detailed disclosure of the components, but MoCRA was set to enforce new guidelines mandating the listing of certain fragrance allergens. However, at the time of this thesis, specific guidelines for fragrance allergen labeling under MoCRA were not yet published by the FDA and therefore cannot be considered (66, 61).

Additionally, all cosmetic labels must bear contact details or electronic contact information of the RP. This ensures that consumers can easily report AE, enhancing post-market surveillance and safety monitoring (26). Cosmetic products, such as liquid products intended for oral or vaginal use, must also comply with special requirements for tamper-proof packaging to safeguard product integrity (67).

Finally, companies must ensure that basic labeling requirements are met, including:

- A list of ingredients in descending order of concentration using INCI nomenclature
- Clear instructions for use and any necessary warnings or precautions

- ❖ The net quantity of the product content
- ❖ Product identity and function (e.g., moisturizer, shampoo)

In summary, while MoCRA increases the transparency and safety of labeling and packaging, particularly for fragrance declarations in the future, it also imposes stricter standards on companies to ensure compliance with FDA and FTC regulations (68, 37). The FDA emphasizes the importance of packaging and labeling for cosmetics, ensuring that all claims are truthful and not misleading, as misbranded products are prohibited.

3.4. Registration and Listing Process in the USA

As already stated in section 3.2 the use of the Portal Cosmetics Direct system is mandatory as it replaces the previously voluntary use of the VCRP. With the implementation of Portal Cosmetics Direct, several new requirements are imposed on cosmetic companies, except for small businesses (69, 27) (For the detailed description of the registration and listing process see ANNEX III).

The shift to mandatory registration and product listing grants FDA increased visibility in the cosmetic market, allowing more effective post-market surveillance and quicker responses to safety concerns. In addition, it enables FDA to maintain an up-to-date database of facilities and products, which can be used for inspections, recalls, or investigations of AE in the future (70).

Companies must register their facilities and list their products within the timeframe as mentioned in ANNEX III, and non-compliance may result in enforcement action, including a warning letter, product recalls or restrictions on the marketing of non-compliant products (71).

In conclusion, the Cosmetics Direct Portal is a key advancement in USA cosmetics regulation, replacing the VCRP with a robust and authoritative system designed to ensure better product safety and compliance.

3.5. Compliance Obligation in the USA

3.5.1. Cosmeticovigilance in the USA

As already mentioned in section 3.2, post-marketing surveillance is one of the key elements in the supervision of the safety of cosmetic products. Cosmeticovigilance refers to the systematic collection, evaluation, monitoring and reporting of AE related to cosmetic products (72).

Here, an AE is defined as "any health-related event associated with the use of a cosmetic product that is adverse" (73). In contrast, a SAE "*means an adverse event that results in death; a life-threatening experience; inpatient hospitalization; a persistent or significant disability or incapacity; a congenital anomaly or birth defect; an infection; or significant disfigurement (including serious and persistent rashes, second- or third-degree burns, significant hair loss, or persistent or significant alteration of appearance), other than as intended, under conditions of use that are customary or usual; or requires, based on reasonable medical judgment, a medical or surgical intervention to prevent an outcome…* " (74). The primary function of a cosmeticovigilance system is to facilitate the reporting of AE, which includes establishing a point of contact and providing reporting forms. Additionally, the system involves assessing these reports through processes such as signal detection, validation, and evaluation. Furthermore, it incorporates risk management measures, which may include issuing safety alerts and implementing potential product recalls (75).

Under MoCRA, the RP is required to report any SAE related to the cosmetic product market in the USA and it must be submitted to the FDA within 15 business days after receiving the information by the RP. The submission must include a copy of product label, or a sales packaging of the cosmetic product (41, 43). Moreover, if new medical information regarding the SAE becomes available within 12 months of the initial report, this must also be submitted to the FDA (76).

The records should be maintained by the RP for a period of six years, except for small businesses. This exception does not apply if the small business is involved in the production of "special-use cosmetic". For all other small businesses, they only have to keep the documents for three years (77). The FDA is authorized to access these records, ensuring

compliance and enabling effective post-market surveillance (78). In cases where a SAE raises concerns about the safety or marketability of a product, such as when a cosmetic product is misbranded or deemed unsafe, the FDA has the authority to demand a recall or the discontinuation of sales (79) (for details see next section 3.5.2.).

However, the full scope of the cosmeticovigilance system is not yet fully known, as there are neither detailed requirements nor guidelines from the FDA. At the moment, the FDA has not yet issued any forms specifically for cosmetic products and the general FDA's Adverse Event Reporting System should be used for reporting (9). Also questionable at this point in the thesis is how to deal with social media and the potential side effect reports contained therein.

In summary, cosmeticovigilance involves the collection and reporting of AE related to cosmetic products, with SAE required to be reported to the FDA within 15 business days. The system includes risk management measures like recalls, and the FDA can demand product withdrawals if safety concerns arise and thus leads to safer cosmetic products for its consumers.

3.5.2. Audit, Recall and Withdrawn of Registration in the USA

As mentioned before, in order to ensure compliance, the FDA may conduct inspections or audits of safety records maintained by the RP (80). MoCRA enables the FDA to obtain and copy certain records about a cosmetic product, including safety records in case of safety concerns (9).

Although the FDA is not directly authorized under the FD&C Act to initiate a mandatory recall of a cosmetic product, the MoCRA has significantly strengthened the agency's role in this area. Under MoCRA, the FDA can formally request a company to recall a product if there is a substantial safety concern, such as the presence of harmful ingredients or misbranding. In addition to making such requests, the FDA now plays an active role in overseeing the recall process. This includes monitoring the progress of recalls, ensuring that companies adhere to appropriate procedures, and verifying that the affected products are effectively removed from the market (71). While most recalls are conducted voluntarily by

companies in response to FDA requests, this increased oversight ensures a higher level of consumer protection and accountability.

In conclusion, this enforcement mechanism strengthens consumer protection and ensures that unsafe products are promptly removed from the market.

3.6. Overview of Federal Regulation of Drug Products in the USA

At this point, only a general overview of drug product regulations will be provided, as the focus here is to differentiate them from cosmetic products. Additionally, this section highlights areas where similarities with pharmaceutical legislation have emerged due to changes introduced by MoCRA.

In the USA, drugs must receive pre-market approval from the FDA through the New Drug Application process, and are governed by the FD&C Act in Title 21, which sets out requirements for the safety, efficacy, and labeling (74).

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*"(81).

Table 1 below highlights important similarities between the requirements of cosmetic products and drug products in the USA on a legal basis, safety requirements, international obligations, post-marketing surveillance, labeling and advertising, and compliance with manufacturing practices.

Table 1: Similarities of the requirements between cosmetic products and drug products in the USA

Issue	USA Cosmetics	USA Drugs
Legal Basis	FD&C Act	FD&C Act
Regulatory oversight	FDA FTC	FDA
Safety requirements	No clinical trials required, but safety evidence is mandatory (e.g. toxicological data or scientific evaluations)	Clinical trials for safety and efficacy are mandatory
Obligation for foreign counties	US Agent*	US Agent
Post-Market Surveillance	Cosmeticovigilance Less intensive monitoring, but companies are responsible for product safety.	Pharmacovigilance Intensive monitoring and mandatory reporting of adverse events
Labeling and Advertising	Misleading claims prohibited; labeling must be clear but less detailed	Strict regulations for package inserts, warning, and advertising claims
Manufacturing Practices	GMP compliance*	Strict adherence to GMP

**except for small business*

These similarities as shown in Table 1 illustrate that while the regulatory intensity differs, both product categories share the overarching goal of ensuring consumer protection and product safety. The introduction of MoCRA has significantly strengthened the regulatory framework for cosmetics in the USA. In brief, this includes stricter safety requirements, enhanced post-market surveillance obligations, and improved transparency for both authority and customer, aligning cosmetic regulation more closely with pharmaceutical standards (9, 82, 56).

4. Federal Regulation of Cosmetic Products in the European Union

4.1. History of Cosmetics Products under EU Regulation

First, the development of the regulatory framework for cosmetic products is examined in more detail. In particular, the key milestones that have shaped the legal and regulatory framework for cosmetic products are discussed. Furthermore, the most important events and changes in legislation have been graphically illustrated to provide a clear overview of the main developments in cosmetics regulation in the EU. The following timeline in Figure 5 illustrates the regulation of cosmetic products in the EU and provides a visual representation of the most important regulatory milestones, including the introduction of Council Directive 76/768/EEC, EU Regulation No. 1223/2009 and the ban on animal testing. The respective milestones will be discussed in more detail later and the main changes will be highlighted.

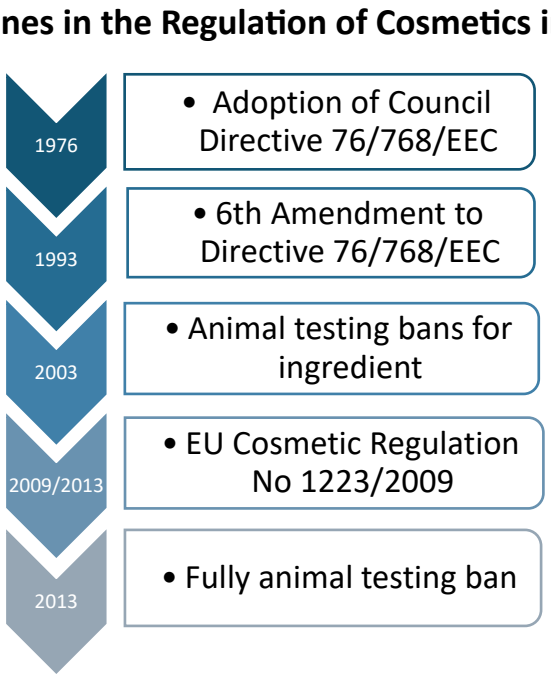

Figure 5: The image illustrates the key milestones in the regulation of cosmetic products in the EU, including the introduction of Council Directive 76/768/EEC, EU Regulation No. 1223/2009, and the ban on animal testing.

As in the USA, the regulation of cosmetic products in the EU has a long history. The harmonization of Member States (MS) legislation on cosmetic products began with Council Directive 76/768/EEC, which came into force on 27 July 1976. The primary objectives of this

directive were to harmonize national regulations, ensure consumer safety, and remove barriers to trade within the EU. It included a definition of cosmetic products, a negative list of prohibited substances, and positive lists of authorized preservatives, colorants, and UV filters (83, 84).

In 1993, the 6th Amendment of Council Directive 76/768/EEC came into force. This most important amendment enhanced the key principles of the EU Cosmetics Regulation, for instance mandatory safety assessment, technical information file, representation by an RP and full ingredient labelling using INCI nomenclature (84, 85).

This directive was replaced by EU Regulation No 1223/2009, which fully entered into force on 11 July 2013. The regulation introduced significant updates, including:

- The requirement that certain ingredients, such as colorants, preservatives, and UV filters, must be explicitly authorized before use (86).
- The establishment of a centralized reporting system, the Cosmetic Product Notification Portal (CPNP), for notifying authorities about products before they are placed on the market (87).

Since 2013, a complete ban on animal testing for cosmetics, both for finished products and their ingredients, as well as a marketing ban on products tested on animals is implemented (88). The EU Cosmetic regulation is described thoroughly in the section 4.2, providing an overview of the regulation in more detail.

Overall, the regulatory framework for cosmetic products in the EU has evolved over time, introducing key measures such as safety assessments, detailed requirements for ingredients, and a ban on animal testing. Important changes include the establishment of a centralized notification system and the implementation of mandatory labeling requirements.

4.2. Overview of the Federal Regulation of Cosmetic Products in the EU

As already mentioned in 4.1, the marketing of cosmetic products in the EU is regulated by Regulation (EC) No 1223/2009. The regulation defines a cosmetic product as "*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 odours*" (89). Similar to the USA, the RP holds a wide range of responsibilities, these aspects and task of compliance obligation will be discussed in more detail (see section 4.3.1 and section 4.5). Another important task is the maintenance of the safety substantiation, due to the significance this will be examined in detail (see section 4.3.3.)

Cosmetic products must be notified thorough the CPNP before being placed on the market, ensuring transparency and regulatory oversight (87, 90)(see section 4.4 and ANNEX V).

In addition, the EU regulation defines the requirements for the formulation of cosmetic products and strictly regulates the ingredients used in cosmetics. The requirements for ingredients are strict as significantly more substances are banned from being used in cosmetic products in the EU. This becomes clear from the negative list of banned substances as listed in Annex III , as well as positive lists for approved preservatives, colorants, and UV filters as listed in Annex II of Regulation (EC) No 1223/2009 (91, 92) (see also section 4.3.2).

Generally, it is mandatory that the companies follow the principles of GMP laid down in ISO 22716:2007 Cosmetics-Good Manufacturing Practices (82) (See section 4.3.4 for more details).

As in the USA, there are several requirements for the labeling of cosmetic products. The regulation establishes comprehensive labeling requirements, such as:

- Listing ingredients using the International Nomenclature of Cosmetic Ingredients (INCI) (93)
- Displaying clear instructions for use and precautions (94)

- Highlighting allergens that might be present (95)

The classification of a product as a cosmetic or medicinal product depends on a case-by-case assessment by the RP and is based on the product's characteristics such as the intended use, the mechanism of action, and how the product is marketed (96, 97). As the packaging and labeling is also associated with advertising, the labeling requirements (see section 4.3.5.).

Another point that should be considered is that a product intended to clean or perfume the skin is classified as a cosmetic, while a product with therapeutic claims, such as treating skin conditions like acne, may fall under medicinal product regulation. In section 4.6 a short overview of the regulation of medicinal products will be given.

In conclusion, the marketing of cosmetic products in the EU is regulated by specific regulations that define cosmetic products, mandate safety substantiation, and require notification through CPNP before market placement, while also imposing strict ingredient regulations, GMP compliance, and comprehensive labeling requirements, with a case-by-case assessment to distinguish between cosmetic and medicinal products.

4.3. Pre-Market Requirements for Cosmetic Products in the EU

4.3.1. Responsible Person in the EU

As highlighted earlier in section 4.2., the RP holds a significant role and must thus be explored in detail. The RP is defined as "*a legal or natural person"* who is designated within the community and must be located in the EU (96). Moreover, the RP acts as the central point of contact between the company and the EU regulatory authorities, ensuring compliance with the EU Cosmetic Regulation (EC) No 1223/2009.

Numerous responsibilities are assigned to the RP, including but not limited to:

- Classification of a product as a cosmetic or medicinal product depending on a case-by-case assessment, based on the formulation of the cosmetic and its characteristics (96) (for further details see 4.3.2 and 4.3.5).

- Compiling and maintaining cosmetic product safety reports (CPSR) and the Product Information File (PIF) (98). Given the importance of the CPSR and PIF, an overview of the content will be addressed (see section 4.3.3. and ANNEX IV).
- Ensuring that the cosmetic product is manufactured in compliance with GMP standards, specifically ISO 22716:2007 (99, 100, 82). Once again, due to the importance of GMP, a more detailed description of the requirements is provided under section 4.3.4.
- Notification through the CPNP before placing the cosmetic product on the market (87, 101). The notification process will be presented (see section 4.4. and ANNEX V).

Beyond that, the RP must ensure compliance with labeling requirements. These requirements will be explained in detail in section 4.3.5. Moreover, the RP is responsible for facilitating the cooperation with regulatory authorities in case of inspections and responding to consumer complaints or AE (A description of the obligation of the AE reporting can be found in section 4.5.1 and requirements of audit, recall and withdrawn are presented in section 4.5.2).

Also for imported products the RP has to verifying that they meet all EU regulatory standards (102).

To summarize, the RP holds a central role in ensuring compliance with the EU Cosmetic Regulation, overseeing product classification, safety reports, GMP standards, and labeling requirements. He is acting as the primary contact with regulatory authorities while also managing the notification process, consumer complaints, and ensuring imported products meet EU standards and thus contributes significantly to the safety of cosmetic products.

4.3.2. Product Formulation in the EU

As mentioned above in section 4.2, compared to the USA, the EU imposes stricter regulations on cosmetic formulations. This becomes particularly clear as the EU bans significantly more ingredients than the USA. Annex II and Annex III of Regulation (EU) No 1223/2009 list over 1580 substances that are either completely banned or strictly regulated for use in cosmetics (103). Additionally, positive lists in Annexes IV to

VI of 1223/2009 specify permitted substances, such as colorants, preservatives, and UV filters, which can only be used under certain conditions (104, 105). These positive lists ensure that only scientifically evaluated and safe ingredients are included in cosmetic formulations.

For cosmetic products containing nanomaterials, additional requirements apply. These nanomaterials must be specified and notified to the European Commission (EC) six months before the cosmetic product is placed on the market as this ensures a thorough evaluation of their safety. However, this requirement does not apply to nanomaterials used as colorants, UV filters, or preservatives, which are already listed in the positive lists as mentioned before (87, 104, 106). Comparable with the USA, all cosmetic formulations in the EU must undergo a safety assessment as described in section 4.3.3, which evaluates the potential risks associated with the cosmetic products ingredients and their interactions. This ensures the safety of the product for consumers under normal and foreseeable conditions of use (97, 107).

In the EU, regulatory authorities emphasize the precautionary principle regarding the cosmetic product formulation, which is evident in the extensive banned substances list and the detailed requirements for nanomaterials (106, 91, 92). In conclusion, the EU imposes stricter regulations on cosmetic formulations than the USA, with a significantly larger list of banned substances, detailed controls on permitted ingredients, additional rules for nanomaterials, and a focus on comprehensive safety assessments and precautionary principles.

4.3.3. Safety Substantiation and Animal Testing in the EU

As previously mentioned in section 4.2, the safety substantiation of a cosmetic product is closely associated with the PIF. The RP is obligated to maintain one for each cosmetic product. The obligation to retain this information file ends 10 years after the last batch of the cosmetic product was placed on the market (108). The PIF must be made readily accessible in electronic or other format and in a easily understandable language at the address mentioned on the label for the competent authority (CA) of the MS (98). A detailed description of the content of the PIF is provided in ANNEX IV.

To ensure the safety of a cosmetic product, the RP must guarantee that a comprehensive assessment is conducted before the product is placed on the market (107). This safety assessment must be performed by a safety assessor holding a diploma or equivalent degree, e.g. a theoretical and practical qualification in pharmacy, toxicology, medicine or similar recognized as equivalent by an EU MS. This ensures that the assessment is conducted by individuals with the necessary theoretical and practical expertise (109).

Beyond that, cosmetic product safety testing includes the preservation challenge test to evaluate microbiological stability, tests for stability under anticipated shelf-life conditions to ensure product quality, and assessments of physicochemical properties of substances and mixtures. Additionally, products undergo impurity and trace analysis to confirm the absence of prohibited substances and evaluate packaging material stability. Exposure assessments calculate the potential impact on users, considering toxicological effects, particle sizes, and secondary exposure risks, such as inhalation or ingestion. For microbiological quality, specific tests focus on products intended for sensitive areas, including eyes, mucous membranes, and damaged skin (93).

Important to mention is, that all non-clinical safety studies used to substantiate product safety must adhere to Good Laboratory Practice (GLP) principles or other international standards recognized as equivalent by the EC or the European Chemicals Agency (110). Compliance with GLP ensures that studies are conducted with transparency, reproducibility, and reliability.

In the EU, animal testing for cosmetic purposes is strictly prohibited, both for finished products and their ingredients. This includes:

- A testing ban: No animal testing may be conducted within the EU to assess the safety of finished cosmetic products or their ingredients.
- A marketing ban: No marketing for finished cosmetic products and ingredients tested on animals in EU (111, 88).

In short, the safety substantiation of cosmetic products in the EU is closely linked to the PIF, which the RP must maintain for each product. The safety assessment must be conducted by qualified professionals and includes various tests such as microbiological, stability, and

exposure assessments, while adhering to GLP, with a strict ban on animal testing for both products and ingredients.

4.3.4. Good Manufacturing Practices for Cosmetic Products in the EU

As already mentioned in section 4.2, all cosmetic products marketed in the EU must comply with the GMP requirements as outlined in the relevant EU regulations. The RP is responsible for following the relevant harmonized standards established within the EU, specifically ISO 22716:2007, which provides guidelines for the production, control, storage, and shipment of cosmetic products (82, 99).

These guidelines ensure that cosmetic products are produced under conditions that guarantee:

- Product quality and safety: All processes are designed to produce products that meet safety standards and are free from contaminants.
- Consistency and reproducibility: Production processes must be well-documented and consistently applied to ensure uniformity of the products.
- Traceability: Ingredients must be traceable from suppliers, through production, to the final product, ensuring that the source and quality of each ingredient are known and meet regulatory standards.
- Hygienic practices: Production facilities must meet strict hygiene and sanitation standards to avoid contamination of products.

In brief, all cosmetic products marketed in the EU must comply with GMP requirements and ISO 22716:2007, ensuring product quality, safety, consistency, traceability, and hygiene.

4.3.5. Packaging, Labelling and Advertisement in the EU

All information on the label must be provided using the language of the country where the product is sold to the end user (112). Similar to the USA, cosmetic products may be

marketed only if their containers and packaging display the details in a clear, permanent, readable, and noticeable format (see ANNEX V) (113).

As stated before, packaging and labelling are important as the advertisement is closely linked. The criteria for the rationale for claims used in context with cosmetic products is laid down in commission regulation (EU) No 655/2013. The term claim refer to words, illustrations or text, names, figures or other indicate either explicitly or implicitly product characteristics or functions in labeling (114). Just as in the USA, it is prohibited to use claims, or other representations that suggest properties or functions the products do not possess (115). Any claim made for a cosmetic product must be based on evidence and be truthful and in line with legal requirements. Furthermore, the advertisement must meet the common criteria of honesty and fairness. For example, ingredient claims that refer to the properties of a particular ingredient should not imply that the final product has the same properties if this is not the case. Also in the EU, the claim “contains moisturizing Aloe Vera” or the prominent image of Aloe Vera must be avoided if the product itself has no moisturizing effect (116).

To sum up, packaging and labeling are crucial for cosmetic products, and all information must be in the language of the market where the product is sold. Claims made in advertisements must be truthful, evidence-based, and align with legal requirements, with false or misleading claims prohibited.

4.4. Notification Process in the EU

As highlighted in section 4.2 already, the registration process is now described in more detail. The CPNP is a reporting system set up to implement Regulation (EC) No 1223/2009. It provides a centralized platform for RP to notify the EC via the CPNP of cosmetic products before they can placed on the market in the EU (87, 101). The notification must be submitted electronically through the CPNP, which makes it easier for authorities to monitor, verify the safety and compliance of cosmetic products on the market (101). This information must be provided in a clear and understandable language for the MS, where the product is being marketed (98) (see in ANNEX VI).

4.5. Compliance Obligation in the EU

4.5.1. Cosmeticovigilance System in the EU

As noted in section 4.2, companies involved in manufacturing, importing, or distributing of cosmetic products are obliged to report any serious undesirable effects (SUE) to the relevant authorities. SUE refers to any health-related event associated with the use of a cosmetic product that results in serious consequences, such as death, hospitalization, significant disability, or permanent damage (e.g., severe allergic reactions, burns, or significant skin reactions) (117).

Similar to the USA, a cosmeticovigilance system must be implemented to fulfill this obligation as this system is a crucial component of the post-market safety monitoring of cosmetic products. Companies are required to set up effective systems for identifying, reporting, tracking, and investigating any SUEs, including those reported by consumers.

The cosmeticovigilance system should include:

- A reporting system for SUE, ensuring that they are reported to CA within the required timeframe of 15 days
- A documentation and investigation process to assess the cause of the undesirable effects and take corrective actions, if necessary
- A method for communicating updates and safety information to consumers and relevant stakeholders, including recall procedures or product safety warnings

Additionally, all relevant safety data and SUE reports must be stored and maintained as a part of the PIF for each cosmetic product (118, 117).

In summary, a cosmeticovigilance system must be in place to monitor, document, and investigate SUE, including storing all relevant safety data as part of the PIF by the RP.

4.5.2. Audit, Recall and Withdrawn of Registration in the EU

A recall is defined as "*any measure aimed at achieving the return of a cosmetic product that has already been made available to the end user*" (119). In a manner similar to the USA, the responsibility of the initiation of a recall lies with the RP. Any cosmetic product placed on

the market by an RP that is believed or suspected to not comply with the regulation must have corrective actions taken immediately to ensure its compliance, be withdrawn, or be recalled, as appropriate (120).

The RP must document the recall action and notify the relevant authorities of the recall, providing details about the product, the reason for the recall, and the corrective measures taken. If the RP is uncertain about the level of risk posed by the product, they must work closely with the CA to assess the situation and implement effective measures (121, 122).

These measures are intended to ensure that the affected product(s) are withdrawn from the market, recalled, or that the availability of the products is otherwise restricted (123).

In conclusion, a recall involves removing a non-compliant cosmetic product from the market, initiated by RP, who must notify authorities and take corrective actions. If unsure about the risk, the RP works with the CA to address the issue.

4.6. Overview of the Federal Regulation of Medicinal Product in the EU

At this stage, a general overview of the EU regulations for medicinal products will be provided, as the primary focus here is on differentiating them from cosmetic products. In addition, the key similarities between the two regulatory frameworks will be highlighted, offering a clearer understanding. In the EU, the approval of medicinal products is primarily governed by the Directive 2001/83/EC and Regulation (EC) No.726/2004 which regulates the authorization of medicinal products and establishes the European Medicines Agency (EMA).

DIRECTIVE 2001/83/EC defines medicinal products as "*Any substance or combination of substances presented as having properties for treating or preventing disease in human beings*" or "*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*" (124). Here, again, it becomes clear that the respective

definitions of medicinal products and cosmetic products differ from each other due to their intended effect and purpose.

In contrast to cosmetic products, medicinal products are subjected to strict clinical trials to demonstrate their safety, efficacy, and quality (125). Once approved, they must undergo post-market surveillance through pharmacovigilance programs to continuously monitor their safety and effectiveness (126).

Table 2 below highlights important similarities between the requirements of cosmetic products and drug products in the EU.

Table 2: Similarities of the requirements between cosmetic products and drug products in the EU

Similarities	EU Cosmetics	EU Medicinal Product
Legal Basis	Regulation (EC) No 1223/2009	Directive 2001/83/EC Regulation (EC) No 726/2004
Regulatory oversight	EC	EMA
Safety requirements	Safety assessment based on ingredients	Clinical trials regulation 536/2014
Obligation for foreign counties	Responsible Person must be located in the EU	Qualified Person must be located in the EU
Post-Market Surveillance	Cosmeticovigilance	Pharmacovigilance
Labeling and Advertising	Specific labeling requirements (INCI, allergens) Regulation (EU) No 655/2013	Strict labeling and advertising regulations
Manufacturing Practices	GMP ISO 22716	GMP Directive (EU) 2017/1572

These similarities, as shown in Table 2, show that both product categories are subject to a similarly high level of regulation. This is particularly the case for compliance with the safety requirements and GMP Guidelines. Overall, EU pharmaceutical legislation defines medicinal products as substances used to treat or prevent disease and requires rigorous clinical trials and post-marketing surveillance and the overall objective of ensuring consumer protection and product safety is achieved.

5. Comparison of the Cosmetic Products Regulations in the USA and EU

This chapter provides a comparison of the specific requirements outlined in the regulations governing cosmetics in the USA and the EU. A comparative look at the cosmetic regulations between the two regions is provided in Table 3, focusing on the key governing laws and the enforcement bodies involved.

Table 3: Overview of the general requirements for cosmetic products in the USA and EU

Requirement	USA	EU
Regulation	Title 21 Food and Drugs MoCRA, Fair Packaging and Labeling Act	EU Cosmetics Regulation EC no 1223/2009
Regulatory Bodies	FDA FTC	EC
Advertising and Claims	Misleading claims are prohibited	Misleading claims are prohibited
Formulation	No UV filters	UV filter under restriction

It is worth noting that even prior to the introduction of MoCRA, both countries placed significant emphasis on ensuring that advertising claims were well-founded and truthful.

A more detailed analysis of the changes in US regulation as a result of MoCRA compared to the EU legislation is presented in Table 4 below.

Table 4: Overview of stricter requirements resulting from the MoCRA in USA compared to EU

Requirement	USA	EU
Responsible Person	Yes	Yes
Safey substantiation	Yes**	Yes
Nanomaterial	Safety testing should be part of the safety assessment	Regulated
Animal testing	Not required	Not allowed (full ban)
GMP Compliance With Guidelines	Future compliance required with GMP Guideline under preparation from FDA*	Compliance required with GMP ISO22716:2007

Requirement	USA	EU
Labelling	Must follow PFLA, detailed listing of fragrance	Must follow EU Cosmetics Regulation
Registration/Notification with Authority	Yes*	Yes
Format	Registration with Cosmetic Direct	Registration with CPNP
Cosmeticovigilance	Yes	Yes
Recall Condition	Can be mandatory requested by the authority	Can be mandatory requested by the authority
Obligation for foreign countries	US Agent	Responsible Person must be located in the EU

** Except for small businesses*

*** Asbestos testing for talc containing products*

Table 4 compares the most important regulatory requirements for cosmetic products in the USA and the EU. It covers several areas, including RP, safety assessments, the handling of nanomaterials, regulations on animal testing, GMP compliance, labeling requirements and registration with the competent authorities. The comparative analysis, as summarized in Table 3 and Table 4, demonstrates how both regions approach the regulation of cosmetic products with an emphasis on safety, transparency, and consumer protection, yet they differ in the scope and enforcement of certain requirements.

A major similarity between the USA and the EU is the focus on preventing misleading advertising claims. Both regions prohibit false claims, ensuring that consumers are not misled by inaccurate product information. This shared approach indicates a common interest in upholding consumer rights and maintaining market integrity in both legislations.

However, the regulation of cosmetic formulations and the safety of ingredients reveals a notable divergence between the USA and the EU. In the USA, ingredients like UV filters falls under strict regulation of drugs, whereas the EU does not yet have equivalent restrictions in place. Furthermore, the EU enforces a complete ban on animal testing for cosmetic

products, a measure that the USA does not mandate, as animal testing is not required under MoCRA. This difference underscores the EU's more stringent ethical stance on cosmetic testing, aligning with its broader approach to consumer and environmental protection.

The implementation of MoCRA has brought the USA's regulatory framework closer to European standards, particularly regarding safety substantiation and adverse event reporting. Under MoCRA, mandates a RP, safety assessments, and vigilance mechanisms like the EU's Cosmetic Regulation. However, the USA still maintains more flexibility, especially for small businesses, with some regulations, such as fragrance labeling and GMP guidelines, still under development by the FDA. This creates a regulatory environment that is more adaptable to the needs of smaller companies, offering them leeway in certain compliance areas.

Additionally, while both regions require some form of registration or notification with relevant authorities, the USA has distinct requirements, such as the need for a US agent, whereas the EU mandates that a RP be based within the EU. This difference highlights the regulatory challenges companies face when marketing cosmetics internationally, as businesses must navigate the specific requirements of each region.

MoCRA marks a significant step toward tightening the regulatory framework in the USA, aligning it more closely with the EU's standards. The emphasis on safety, transparency, and consumer protection in both regions reflects a shared commitment to an improvement of the cosmetic products sector. However, the EU remains ahead in terms of regulatory details and enforcement, particularly in areas such as animal testing, GMP compliance, and the handling of nanomaterials.

In conclusion, while both the USA and the EU are moving towards stricter regulations in the cosmetics industry, the EU’s approach remains more comprehensive, with more rigid requirements in several key areas. MoCRA has certainly improved the regulatory landscape in the USA, but it still allows greater flexibility, particularly for smaller businesses, compared to the EU’s more stringent framework. As the FDA continues to develop and finalize regulations under MoCRA, the USA may see further alignment with European standards in the coming years, though the two regions will likely continue to exhibit some differences in regulatory structure and enforcement.

The evaluation in section 6 will provide an overview of how these new pre-market requirements impact companies, with a focus on practical implications and the steps necessary for compliance, especially under the revised regulatory landscape.

6. Evaluation of the Requirements for Small and Medium-Sized Enterprises

As already highlighted, the pre-market and compliance requirements have increased in the USA under MoCRA. The updated requirements pose significant challenges for all companies operating in the USA, profoundly affecting their operational, compliance, and strategic processes. The burden for SMEs in particular will be considered here, as they often have limited resources, both in terms of budget and personnel.

6.1. Product Formulation

As a first step, it is highly recommended to conduct a comprehensive and thorough review of the current formulation of the cosmetic product. This process involves carefully assessing all the ingredients and their compliance with the updated regulatory requirements, as outlined under MoCRA. Furthermore, this review should include ensuring that all ingredients, e.g. fragrances used in the formulation, are fully disclosed and compliant with the new labeling requirements that will follow soon. This will also be discussed in section 6.4 below.

Especially, for SMEs, this could mean:

- Documentation burden: Review of the current formulation, identify potential critical ingredients, create detailed lists of ingredients
- Infrastructure burden: Adaption in production, additional storage capacity and investment in formulation management and documentation systems
- Employees burden: Hire additional employees or an external consultant, particular in the area of regulatory, quality control and development
- Financial burden: Medium

Under MoCRA, ingredients such as fragrance must be listed on the label. In the short term, the review of the formulation may lead to investments, as the existing composition and critical ingredients need to be identified and assessed. If necessary, changes to the formulation should be considered. This could result in high future costs due to additional testing and label updates.

6.2. Safety Substantiation

It is important to emphasize that a company was also obliged to ensure the safety of its cosmetic products in the past. However, under MoCRA, the requirements of the documented safety substantiation have been extended as the FDA mandates scientifically supported safety testing records to validate product safety. As a result, scientific testing and additional documentation may be carried out.

Especially, for SMEs, the updated proof of safety substantiation could mean:

- Documentation burden: Revising or creating documentation of testing
- Infrastructure burden: Establishment of robust documentation system
- Employees burden: Hire additional employees or an external consultant, particular in regulatory, quality control and development of cosmetic products
- Financial burden: Medium-High

Under MoCRA, the requirement of detailed documented safety substantiation must be implemented as soon as possible, whereas companies can rely on existing safety data from individual ingredients and similar formulations. This can lead to a high investment in the short term as the existing documentation must be checked for completeness and, if necessary, additional documentation must be requested or performed, much likely at contract laboratories. It may be necessary to repeat testing or carry out further testing.

In the long term, this might be a significant cost factor. For example, outsourcing testing and compliance checks conducted by external laboratories may involve high investment. These services can be expensive, particularly if frequent or specialized testing is required to meet regulatory standards of safety substantiation. In addition, dependence on external providers can lead to price fluctuations or additional costs for urgent tests, which represents a considerable financial burden in the long term.

6.3. Compliance with GMP

As stated, in section 3.3.4, the implementation of GMP is now one of the key requirements under MoCRA and possibly the most significant challenge for SME. However, as already

mentioned, there is an exception here for small businesses that do not have to be GMP compliant but recommended to be voluntary in compliance with GMP. However, the scope of these requirements is currently still under discussion at the FDA. Nevertheless, there is a draft version that might serve as a guide. As already mentioned, for reasons of harmonization, it should be assumed that they will have the same scope as the EU.

Compliance with GMP may entail for SME:

- Documentation burden: Revising or creating documents
- Infrastructure burden: Room and equipment upgrades
- Employees burden: Comprehensive training programs to ensure compliance and/or assignment of consultant
- Financial burden: High

The requirement of GMP compliance must be implemented in the long term. Compliance with GMP has far-reaching significance in the facility, manufacturing process and storage as all aspects must be carried out under standardized conditions. Among other, the facilities must be suitable for this purpose, the processes have to be standardized, and employees must be intensively trained. In the short term, this led to high costs, as new equipment might be acquired, additional training for employees must be carried out and comprehensive standardization must be implemented. Beyond that, it is possible that external consultants need to be engaged to navigate the compliance with GMP.

In the long term, it also could be a major cost factor as the maintenance of a GMP compliant system requires constant training of employees, maintenance of documentation and quality control. These points make it clear that it is the largest burden for small businesses. However, compliance with GMP can lead to possibilities that will be later discussed in more detail.

6.4. Packaging, Labeling and Advertisement

As highlighted in section 3.3.5, the revised labeling regulations require the mentioning of the RP and include the detailed declaration of fragrance or allergens, if applicable. For that reason, a comprehensive review of the label and labelling must be performed to ensure

that the RP is mentioned with detailed contact data. Although there is not yet a final specification for the detailed mentioning of the fragrance, as a precautionary measure, potential fragrances ingredients should be identified to proactively fulfill the upcoming requirements. This may require redesigning the product packaging and labeling.

It could imply for SMEs:

- Documentation burden: Revising or creating packaging and labeling artwork
- Infrastructure burden: Revising existing stock to comply with the new requirements
- Employees burden: Training programs for employees and/or assignment of consultant
- Financial burden: Low -Medium

The mentioning of the RP on the labeling must be implemented as soon as possible. In the event that the packaging and labeling does not meet the requirements, a revision of the packaging and labeling must be implemented. A higher investment may be needed as the artwork needs to be checked or revised and outdated packaging destroyed. This can be done internally or may require the use of external consultants or service providers.

In the long term, the requirements of packaging and labeling must be checked regularly. However, this does not require as many resources and the investment can be classified as low.

6.5. Facility Registration and Cosmetic Product Listing

As described in section 3.4, facilities and cosmetic products must now be listed with the FDA, which requires the use of the Cosmetics Direct Portal. However, there is also an exception here for small businesses, which do not have the obligation to register and list their cosmetic products. The Cosmetics Direct Portal has been introduced and must now be regularly maintained.

The key challenges for SME include:

- Documentation burden: Request and receive necessary information internally
- Infrastructure burden: Registration with the portal required

- ❖ Employees burden: Training for employees and/or assignment of consultant
- ❖ Financial burden: Low

Compared to other requirements, the challenges for SME are relatively low.

It is necessary to make an initial effort to register the company and the cosmetic products. This may result in training for the employees to enable them to operate the system, or the assignment of consultants or service providers. In the long term only, a small financial investment is required, as little effort is needed to maintain this database. However, the use of Cosmetics Direct Portal is a small burden for small businesses. For that reason, the implementation of use of the portal can lead to possibilities that will be later discussed in more detail together with compliance with GMP.

6.6. Cosmeticovigilance System

As already mentioned in section 3.5.1, MoCRA requires the introduction of a robust cosmeticovigilance system. This is also a major challenge, especially for SMEs, especially if this system must be newly implemented. In addition to the initial set-up, the system also has to ensure ongoing monitoring, signal detection and reporting of AE, which requires significant resources. SMEs may struggle to find time and financial resources required to set up and maintain such a system, increasing the complexity and cost of their operations.

This could SMEs result in:

- ❖ Documentation burden: Establishment of documentation, e.g. forms
- ❖ Infrastructure burden: Establishment of robust cosmeticovigilance system
- ❖ Employees burden: Recruitment of specialists, training programs for employees and/or assignment of consultants
- ❖ Financial burden: High

In the short term, the implementation of a cosmeticovigilance system leads to a high financial burden, as the system, processes and documentation must be established and validated. In addition, it must be possible to obtain safety-relevant reports from the market and the exchange with the FDA must be always ensured.

However, this means that high investment costs are expected in the future, as maintaining the system is also costly. This includes not only system updates and optimization but also

ongoing investments in employee training to ensure employees are up to date with regulatory requirements or the assignment of a consultant. In addition, the SME could also consider outsourcing the cosmeticovigilance system to a service provider.

6.7. Audit, Recall and Withdrawn of Registration

As noted in section 3.5.2, the FDA cannot directly mandate cosmetic recalls. However, it is required for a company to be able to perform mandatory recalls on request. For this reason, a robust recall procedure must be implemented.

This may indicate for SME that:

- Documentation burden: Develop clear recall protocols
- Infrastructure burden: Establishment of recall process
- Employees burden: Training program for employees and/or assignment of consultant
- Financial burden: Low

Here again, compared to the other requirements, the challenges for SME are relatively low. It is essential to implement a recall process, which may involve introducing a reliable system and employee trainings in its execution or assigning consultants. However, in the long term, this requires only minimal financial investment, as maintaining the recall process involves relatively low ongoing effort.

In summary, particular challenges arise in areas such as product formulation, safety substantiation, GMP compliance, labeling and packaging, registration, cosmetic vigilance, and recall procedures. For SMEs, this often translates into significant documentation efforts, additional infrastructure investments, increased number of employees, and financial burdens. While some requirements, such as registration, are relatively straightforward, others, such as safety substantiation and compliance with GMP standards, necessitate considerable short-term and long-term investments.

7. Analysis of Decision

Based on the knowledge and insights gained so far, recommendations for further steps are now being made on the case study of a USA-based SME, which markets several products with an annual turnover of $750,000 in the USA. The definition of a small business is met and therefore the company does not need to register and list the cosmetic product with the FDA and does not be GMP compliant.

With small businesses, especially with sales of this scale, it can be assumed that there are financial and personnel limitations and these are considered. The implementation of a cosmeticovigilance system alone can lead to small businesses not being able to overcome this burden and therefore having to withdraw their products from the market. The decision to continue business activities in the US market ultimately depends on a precise weighing up the costs of achieving the required compliance. SMEs should conduct an early analysis of the new MoCRA requirements and prioritize important factors such as product formulation, safety assessment and GMP compliance, if applicable. External support from consultants can help to fulfill the regulatory requirements efficiently. Investments should also be made in infrastructure and employee training to ensure compliance with GMP standards and cosmeticovigilance. Continuous adaptation of processes is necessary to keep pace with changing regulations. In the long term, SMEs should develop a strategy that takes into account both short-term requirements and long-term costs and benefits to ensure their competitiveness. Two different approaches are examined and analyzed in more detail below. The aim of this analysis is to discuss the key features, differences and potential advantages and disadvantages of each approach.

7.1. Risk-Averse Strategy

First of all, the risk-averse strategy should be shown and discussed. If there are significant financial restrictions, a risk-averse strategy should be examined in more detail. This assumes that the budget must be adhered to and that investments can only be made in the long term. In this case, it is advisable to only meet the mandatory requirements under MoCRA. Table 5 summarizes the key points of a risk-averse strategy, focusing on financial limitations, investment priorities, and the advantages and disadvantages of adapting to MoCRA

requirements for the US market. Table 5 outlines the key aspects of a risk-averse strategy, focusing on financial limitations, investment priorities, and the advantages and disadvantages of adapting to MoCRA requirements for the US market.

Table 5: Risk-Averse Strategy Overview

Aspect	Details
Financial Limitations	Low budget and long-term investment limitations
Investment Focus	Focus on mandatory requirements, with investments in critical areas like implementation of cosmeticovigilance system, safety substantiation documentation and possibly label updates
Market Adaption	Adaptation only to MoCRA requirements for the US market (No GMP Compliance and Registration/Listing) in order to spreading investments over a longer period
Advantages	Controlled implementation, reduced financial/organizational burden, and minimized errors with new systems (e.g., cosmeticovigilance)
Disadvantages	Limited market reach to the US, missed international market opportunities (e.g., EU), dependency on US market, and potential growth restrictions

Table 5 highlights the key points of a risk-averse strategy, focusing on financial limits, investment priorities, and MoCRA adaptation for the US market without compliance with GMP and registration and listing requirements. If there are clear financial limitations, a risk-averse strategy should be examined in more detail. It is assumed here that the budget must be adhered to and that investments can only be made in the long term. In this case, it is recommended that only the mandatory requirements must be met. Investments should be focused on particular critical areas such as cosmeticovigilance systems, safety testing and updating labels because these need to be implemented in a timely manner. However, consideration should be given to whether the current exemption from certain regulations

allows for sufficient operational profitability. The exclusive adaptation to the MoCRA requirements for the US market offers the advantage of spreading investments over a longer period and aligning processes specifically to one market. This reduces the financial and organizational burden, enables controlled implementation and minimizes errors when introducing new systems such as cosmeticovigilance systems.

Nevertheless, the disadvantage is that if the company attempts to expand its sales or increase its prices, it may face difficulties as soon as the average gross sales are more than $1,000,000 the registration and listing requirements and GMP compliance are mandatory.

Another disadvantage is that it is considerable as the products can only be marketed in the USA, which severely limits the company's geographical reach and growth potential. Opportunities in international markets such as the EU are missing, and dependence on the US market increases the risk of being disproportionately affected by regulatory or economic changes. This could jeopardize competitiveness in the long term.

In conclusion, a risk-averse strategy focuses on meeting only the mandatory MoCRA requirements for the US market, prioritizing areas like implementation of cosmeticovigilance system, safety substantiation and label updates while minimizing costs and organizational burdens. However, this approach limits geographical reach, misses international opportunities, and increases dependence on the US market, potentially restricting growth.

7.2. Risk-Based Strategy

Even the risk-based strategy is based on financial and personal limitations. However, it is assumed that there is more readiness to high short-term investments. The key aspects of a risk-based strategy are shown in Table 6 and will be discussed in more detail below.

Table 6: Risk-Based Strategy Overview

Aspect	Details
Financial Limitations	Low budget, however, readiness to make larger short-term investments
Investment Focus	Focus on mandatory requirements, in addition: Registration and Listing requirement and compliance with GMP
Market Adaption	Compliance with GMP is not mandatory but enhances future grow and global marketing
Advantages	Strengthens credibility, supports expansion into the EU, and offers long-term benefits with regulatory compliance in multiple markets
Disadvantages	Higher short-term investments, increased risk, and potential budget challenges

As shown in Table 6, it is advisable to fulfill all requirements. This is in particular recommended regarding the registration and listing obligation, as this can be fulfilled with minimal effort. Even though GMP compliance is not mandatory and very expensive, implementing such standards strengthens the company's credibility and makes it easier to adapt to future regulatory requirements. Investing in training and bringing in external expertise can help to expand internal knowledge and increase organizational capacity for smooth implementation. The advantage is that GMP compliance can also be used as a strategic advantage. At the same time, this creates the basis for expansion into regulated markets such as the EU, where GMP standards are already a mandatory requirement. One suggestion for GMP compliance here would be to align with the EU standards, as there are no established GMP requirements in the US yet. The EU's GMP framework provides an international recognized and robust standard, making it an ideal foundation for a unified registration strategy. The European cosmetics market, known for its stability, consumer trust, and strict regulatory environment, offers significant growth potential as mentioned

before. Aligning with EU standards facilitates market entry, builds credibility, and strengthens the brand's global appeal. By adopting a harmonized approach to compliance, the company can capitalize on opportunities in the EU while maintaining its presence in the USA.

The disadvantage of this approach is that it involves higher short-term investments, which can strain resources and create financial pressure. Additionally, the higher level of risk means that the expected budget may not be met, leading to potential cost overruns and delays.

In summary, a risk-based strategy focuses on meeting all regulatory requirements, including GMP compliance despite the financial burden. This boosts credibility, supports EU expansion, but involves higher short-term investments and risks. Despite the initial financial burden, a joint registration strategy offers substantial long-term benefits by securing regulatory compliance in multiple markets, enhancing operational efficiency, and unlocking growth opportunities in key regions such as the EU and the USA. This joint registration strategy will be presented in the following section 8.

8. Development of Joint Registration Strategy for the USA and EU

Based on previous insights, a registration strategy will be developed using a hypothetical case study of a US-based small business with an annual turnover of $750,000. The strategy will consider a market analysis to identify in-demand products, with a focus on the growing European trend for natural and organic cosmetics due to increased health consciousness (13).

The first step in developing a new "green" product line, which will be proposed to the US company, includes products with minimal ingredients and sustainable packaging for both the EU and US markets.

- **Aim**: Development and registration of cosmetic products for the USA and EU market.
- **Activities:**
    - Review current regulation of cosmetic products in USA and EU

- Establishment of Target Product Profile (TPP)
- Establishment of cosmetic product formulation
- Design of packaging and labeling
- Establishment of CPSR and PIF according to EU legislation and safety substantiation
- Establishment of cosmeticovigilance system
- Development of marketing and advertising strategy
- Registration of cosmetic product

❖ **Responsible Department:** Regulatory Affairs, Marketing, Research & Development, Production, Quality Management, or Consultant or Service Provider

❖ **Timeframe:** 12-18 months

By following these steps, companies can effectively navigate the complex regulatory environment and ensure that their cosmetic products are safe, compliant and will be successfully registered in both the EU and US markets.

8.1. Milestone 1: Development of a TPP

The development of a TPP can be a useful step in this process. The following key elements as listed in Table 7 should be included in the TPP.

❖ **Aim**: Development of TPP

❖ **Activities:**

- Detailed Review of EU and USA regulations
- Analyses of market
- Discuss formulation and intended use
- Discuss potential design of packaging and labeling
- Discuss potential marketing and advertising strategy

❖ **Responsible Department:** Regulatory Affairs, Marketing, Research & Development, Production, Quality Management, or Consultant or Service Provider

❖ **Timeframe:** 1-3 months

Table 7: Target Product Profile for the cosmetic product

Product name	"AquaBoost Glow" Green Reflects hydration ("Aqua") and essential skin nourishment ("Boost"). "Glow" emphasizes the glow enhancing properties of the formulation
Product type	Facial moisturizer (cream)
Intended use	The cosmetic product helps to reduce skin ageing, provides long-lasting moisture and soothes irritated skin. It protects against environmental influences and strengthens the skin against external stress.
Claims	❖ Anti-Aging (127) ❖ Provides long-lasting hydration (128) ❖ Soothes and calms irritated skin (129) ❖ Protects against environmental stressor(130)
Target audience	Women aged 20-50 normal to dry skin
Formulation	❖ Hyaluronic acid (Moisturizing and skin conditioning) (128) ❖ Retinol (Antioxidant protection)(127) ❖ Glycerin (129) ❖ Aloe Vera leaf extract (Soothing and calming properties) (130)
Formulation standards	❖ Free from parabens and fragrances ❖ Free from PFAS ❖ Free from colorants ❖ Dermatologically tested for sensitive skin ❖ No animal testing for all ingredients in the supply chain ❖ No use of nanomaterial
Packaging	❖ Airless pump for optimal hygiene and preservation in glass bottle
Shelf life	❖ Minimum of 12 months under recommended storage conditions.

Labeling	❖ Language English ❖ Mentioned of RP with detailed contact information ❖ Use of INCI naming convention

This TPP as listed in Table 7 considers the different requirements in the USA and the EU in order to develop a product that is suitable for both markets. It is essential to conduct a thorough examination of the legislation to ensure clear classification of the cosmetic product. For example, a product classified as a cosmetic in the EU may be considered a drug in the USA, such as sun protection products.

8.2. Milestone 2: Implementation of GMP

Although the implementation of compliance with GMP is associated with significant financial burden, it has the highest priority in a joint registration strategy because all products marketed in the EU must be manufactured under GMP (see section 4.3.4).This approach will also ensure that future requirements of compliance with GMP in the USA are met.

- **Aim**: Ensure that the production environment meets GMP standards before starting actual product development and registration.
- **Activities:**
  - Selection and equipping of the production site in accordance with GMP standards
  - Implementation of hygiene and quality control processes
  - Training of employees in GMP requirements
  - Setting up a system to monitor production quality
  - Preparation of documentation for all production processes
- **Responsible Department:** Production, Quality Management and/or Service Provider or Contract Manufacturer
- **Time frame:** 3-6 months prior product development

This implementation would ensure that the product meets the highest safety and quality standards during development and registration. In the short term, production could be outsourced to a contract manufacturer to reduce costs significantly. Partnering with a GMP-certified manufacturer ensures high quality while taking advantage of their specialized facilities and cost-efficiency. However, in the long term, it has to be evaluated whether implementing an in-house GMP facility could be more cost-effective. After the introduction of GMP, it will be possible to continue with the next milestones, such as the safety assessment and registration in the EU and the USA.

8.3. Milestone 3: Analysis and/or Development of Formulation

A detailed analysis and formulation development must be carried out. This involves carefully selected ingredients that meet the legal requirements and regulations in both the EU and the USA. The safety of these ingredients must be evaluated, considering potential risks, toxicological profiles, and known AEs. Furthermore, the formulation must account for banned substances and any specific restrictions on certain ingredients, ensuring adherence to the relevant regulations in both regions.

- **Aim:** Ensure that all ingredients are safe and meet the legal requirements of both markets.
- **Activities:**
    - Careful review or development of the product formulation to identify any necessary safety testing requirements
    - Selecting ingredients that comply with the legal framework in the EU and the USA (see section 3.3.2 and 4.3.2)
    - Assessment of the safety of ingredients and considering potential risks, banned substances and restrictions on use (see section 4.3.2 and 4.3.3)
    - Only use ingredients for which comprehensive safety data sheets are available, obtained through database searches, to reduce the need for extensive toxicology testing by relying on ingredients with proven safety information
    - Document all ingredients and (potential) impurities of the cosmetic product

- **Responsible Department:** Regulatory Affairs Department, (external)-Safety Accessor or Service Provider
- **Time frame:** 6-8 months

Based on the previous information, additional requirements are placed on the formulation for strategic reasons. Aspects, details and the resulting strategic advantage are outlined in Table 8.

Table 8: Establishment of formulation for "AquaBoost" Green

Aspect	Details	Advantage
No UV filter	The use of UV filter leads to drugs regulation in the USA	Registration in EU and USA without additional requirements
No Nanomaterial	Avoid the use of nanomaterials	Reducing testing costs and efforts
No Parabens	Avoid the use of Parabens (preservatives)	Planned Indication for sensitive skin
No Fragrance	Avoid the use of Fragrance	Planned Indication for sensitive skin and additional requirements for listing fragrances
Additives (e.g., preservatives)	Minimize additives such as preservatives due to the product's indication for sensitive skin	Planned Indication for sensitive skin
No Animal testing	Ensure that no ingredients have been tested on animals in the supply chain, and explore alternative suppliers if necessary	Registration requirement in EU

Table 8 shows that avoiding UV filters, nanomaterials, parabens, fragrances and additives has advantages such as simplified registration in the EU and the USA and reduced testing requirements for sensitive skin. In addition, the avoidance of animal testing is emphasized as a prerequisite for registration in the EU. Furthermore, it could be beneficial for strategic reasons to omit ingredients such as UV filter so that the product does not have to be marketed as a medicinal product in the USA. In addition, the use of nanomaterials should be avoided, as this requires extensive testing and thus incurs additional costs.

In summary, the product formulation must comply with EU and US regulations, using safe ingredients and avoiding UV filters. Preservatives should be minimized, and the supply chain must ensure no animal testing as well as promoting sustainability. By ensuring that the formulation meets both standards, companies can mitigate the risks and create a solid foundation for successful registration.

8.4. Milestone 4: Design of Packaging and Labeling

Even if packaging is not required immediately, it is important to ensure that any claims made about the product on the packaging and label are supported by scientific testing. This is essential to avoid losing out on the potential competitive advantages these claims may provide. It is recommended to begin drafting the claims early in the product development process, ensuring they are properly substantiated and ready for marketing.

- **Aim**: Ensure packaging and labeling comply with USA and EU requirements (see section 3.3.5 and 4.3.5)
- **Activities:**
  - Design and check compliance of packaging to be in line with EU and USA requirements
  - Design and checking compliance with labelling in line with EU and USA requirements (language, ingredients, warnings)
  - Ensuring the complete and correct declaration of all ingredients
- **Responsible Department**: Regulatory Affairs Department, Design and Marketing Team (or Service Provider)
- **Timeframe:** 2-3 months

However: Packaging is needed to establish stability data, and the labeling must be final for the establishment of the PIF as stability data and labeling are part of the PIF.

Further design specifications for labeling are listed in Table 9.

Table 9: Additional features in design of packaging and labeling

Aspect	Details	Advantage
Packaging and Labeling Material	Should be sustainable	Highly recyclable, potential appealing for consumer
Packaging	Glass bottle	Recyclability and durability, potential appealing for consumer
Special packaging feature	Pump bottle	Prevents direct contact with the product, reducing the risk of contamination and the need for preservatives

Further design specifications for labeling in accordance with the TPP are shown in Table 9. Sustainable and easy to recycle materials should be used as they are not only environmentally friendly but can also improve the image of a product and make it more attractive to environmentally conscious consumers.

In times of increasing awareness of environmental issues, choosing sustainable materials can also increase consumer confidence in the brand. To further enhance hygiene, a glass pump bottle is ideal, as it prevents direct contact with the product, reducing the risk of contamination and the need for preservatives. Moreover, the packaging must meet the necessary stability requirements to provide the data required for the CPSR, ensuring the product's safety and regulatory compliance (see section 8.5 and ANNEX IV).

In summary, it is important that all product claims are supported by scientific testing to secure competitive advantages and should be drafted as well as reviewed early in the development process. The packaging and labeling must comply with USA and EU requirements. Provide a competitive advantage, sustainable materials, such as glass bottles

with a pump mechanism, are both environmentally friendly and hygienic while ensuring regulatory requirements and stability data for product registration.

8.5. Milestone 5: Establishment of CPSR and Additional Evidence for claims

An equally important step is to confirm the safety of the cosmetic product. This testing process must be carried out to ensure that the product meets the required health and safety standards before it is launched on the market. It is particularly important to emphasize that animal testing must be strictly avoided at all stages of the safety assessment. Today, various alternative methods are available to test the safety and efficacy of cosmetic products, including in vitro tests, in silico and modern skin models. Moreover, for small companies, relocating clinical testing for supporting claims, e.g. “Dermatologically tested for sensitive skin”, to EU countries that offer them at a lower cost could be a beneficial option.

- **Aim**: Carrying out a safety assessment for the product and preparing a CPSR for the product and conducting additional testing for evidence supporting claims to comply with EU regulations
- **Activities:**
  - Review data sheets and search databases to replace ingredients testing
  - Conduct a safety assessment based on CPSR requirements (ANNEX IV)
  - Creation of CPSR
- **Responsible Department**: Research& Development, Safety Accessor and/or Service Provider
- **Timeframe:** 2-3 months

  However: Must be final before the establishment of the PIF as CPSR is a part of the PIF.

Furthermore, the comprehensive safety data gathered through CPSR can be used as substantiation of the product’s safety when registering it in the USA, where the requirements for safety testing are generally less stringent. This makes the CPSR a key document for both European and American markets.

Overall, verifying the safety of a cosmetic product should be done according to CPSR requirements, avoiding animal testing by using alternative methods like in vitro testing, computer modeling, and advanced skin models, with the resulting safety data also serving as proof for regulatory submission in the USA.

8.6. Milestone 6: Establishment of Cosmeticovigilance System and Recall Processes

The establishment of a cosmeticovigilance system is also a very complex process that should be started as soon as possible. Companies need systems to monitor cosmetic safety, address issues, and report adverse events, ensuring compliance with regulations. In addition to establishing the processes, these must also be validated.

- **Aim**: Implementation of cosmeticovigilance system for market-surveillance and compliance with regulations
- **Activities:**
  - Establish system, processes and documentation
  - Validate system and processes
  - Creation of CPSR
- **Responsible Department**: Regulatory Affairs, Quality Managements and/or Service Provider
- **Timeframe:** 2-3 months

  However: Must be final before the registration of a cosmetic product

One potential solution is to engage a service provider to manage the cosmeticovigilance system initially, with the option to establish an in-house system later. The benefit of this approach is quick implementation, but the downside is the high associated costs. To sum up, establishing a cosmeticovigilance system is a complex and urgent process requiring robust systems to monitor product safety, address concerns, and report AEs, with smaller companies possibly opting for a service provider for quick implementation despite the high costs.

8.7. Milestone 7: Establishment of PIF in compliance with EU and Safety Substantiation

The PIF is an important document and requires extensive documentation gathered during the completion of previous milestones, including description of manufacturing process under GMP, detailed description of formulation, safety data of the ingredients, labeling information, CPSR and other necessary materials, and is based on EU regulations.

- **Aim**: Preparation of PIF in compliance with EU regulation.
- **Activities:**
  - Collect and review the documentation for the PIF
  - Establishment of PIF
  - Maintaining of PIF
- **Responsible Department**: Regulatory Affairs, Quality Managements, Safety Assessor, Marketing, and/or Service Provider
- **Timeframe:** 2-3 months

  However: Must be final before the registration of a cosmetic product as all information needed for the PIF must be entered to CPNP Portal

Overall, the PIF is an important document that must be created in accordance with EU regulations and includes information such as the manufacturing process, formulation, safety data, and labeling.

8.8. Milestone 8: Development of Marketing and Advertising Strategy

The goal of this milestone is to create a marketing and advertising strategy for your cosmetic product that complies with the regulatory requirements of both the EU and the US. This ensures legal compliance, avoids fines, and maintains consumer trust. The focus is on adapting promotional materials to prevent unauthorized health or medical claims, while aligning marketing with both regions' regulations.

- **Aim**: Development of a marketing strategy that meets the legal requirements of both markets

- **Activities:**
    - Ensure no unapproved health or medical claims:
    - Adapting marketing material to meet regulatory guidelines
    - Ensuring advertising claims meet both markets' guidelines
    - Review of packaging and labeling
- **Responsible Department**: Marketing and Regulatory Affairs and/or Service Provider
- **Timeframe:** 2-3 months

  However: Should be final before the registration of cosmetic products

In summary, creating a marketing and advertising strategy that complies with the regulatory frameworks of both the EU and the US is crucial for the successful launch and sustainability of your cosmetic product. The activities outlined above will help ensure that all marketing materials are legally compliant, preventing any misleading claims or potential legal issues.

8.9. Milestone 9: Cosmetic Product Registration with EU

Registration can now be completed within the EU, but US companies must appoint a RP based in the EU. This representative ensures compliance with EU regulations and handles the necessary documentation.

- **Aim**: Registration of Cosmetic Product with CPNP in the EU
- **Activities:**
    - Obtaining all information
    - Registration of the product in the CPNP portal, including all necessary information (product details, safety report, manufacturer information)
- **Responsible Department**: Regulatory Affairs and/or Service Provider
- **Timeframe:** 1 month

  However: This step can only be taken when all documents, reports and labeling are available based on PIF.

To sum up, US companies must appoint a PR based in the EU to ensure compliance and handle the registration of cosmetic products with the CPNP portal. This process involves gathering necessary documentation and can be completed within one month, but it requires all reports, labeling, and documents based on the PIF to be available beforehand

8.10. Milestone 10: Cosmetic Product Registration with USA

In parallel to the registration in the EU, the registration in the USA can be prepared. Once completed, these documents can then be used for successful product registration in the USA. Based on CPSR the registration process will be done

- **Aim**: Registration of Cosmetic Product with Cosmetics Direct Portal in the USA
- **Activities:**
  - Obtaining all information
  - Registration of the product in the Cosmetics Direct Portal

- **Responsible Department**: Regulatory Affairs and/or Service Provider
- **Timeframe:** 1 month

  However: This step can only be taken when all documents, reports and labeling are available based on EU PIF.

In summary, the development of a joint registration strategy for a US-based SME selling cosmetics in the EU and US markets involves key steps, including market analysis, creating a sustainable "green" product line, and developing a TPP. The strategy includes product formulation, packaging design, safety substantiation through CPSR and PIF, establishing cosmeticovigilance systems, and creating a marketing strategy. For small companies, developing a successful cosmetic product registration strategy in the US and EU requires careful planning, cross-departmental collaboration and regulatory compliance in both markets. This includes market analysis, sustainable product formulations, safety evidence and effective marketing strategies, all of which can be achieved within 18 to 30 months.

9. Summary and Outlook

Cosmetic products have a long history, originating in ancient civilizations, where they were used for aesthetic and therapeutic purposes. Initially reserved for the upper classes, cosmetic products became more accessible to the broad number of consumers due to industrialization. However, some products contained harmful ingredients, leading to the need for strict regulation of cosmetic products in the USA and in the EU.

The history of cosmetics regulation in the USA began with the FD&C Act of 1938. Under MoCRA, the FDA's authority over product safety, adverse event reporting, and manufacturer requirements were significantly expanded.

Cosmetic products are classified by intended use and ingredients, with exceptions for products like self-tanning lotions and anti-dandruff shampoos. The FDA regulates ingredients for safety, with particular focus on substances like PFAS. Under MoCRA, more stringent safety measures for the cosmetic sector in the US have been introduced, as companies are required to maintain documented safety substantiation for all products, meaning that they must provide evidence supporting the safety of their cosmetics.

MoCRA improves transparency in labeling and packaging, particularly for fragrance declarations, and introduces the "Cosmetics Direct Portal" for better product safety and compliance. Moreover, the companies are requested to implement a cosmeticovigilance system for monitoring and reporting any AEs or safety concerns related to cosmetic products after they are placed on the market to FDA.

In comparison, cosmetic legislation was introduced in Europe with the implementation of the regulatory framework with key milestones such as Council Directive 76/768/EEC and EU Regulation No. 1223/2009. Notable developments include mandatory safety assessments, ingredient labeling, the establishment of the CPNP system, and the complete ban on animal testing for cosmetics, all contributing to increased consumer safety and product transparency with the amendment of 2013. These comprehensive regulations contribute significantly to increased consumer safety and product transparency and make EU regulations much stricter than in the USA.

Both the USA and the EU focus on preventing misleading advertising claims to protect consumers, ensuring product information is accurate. However, they differ in their

requirements of cosmetic formulations and ingredient safety. In the USA, ingredients like UV filters are treated as drugs, while the EU has no similar regulation. The EU also enforces a full ban on animal testing, unlike the USA, where animal testing is permitted.

MoCRA has aligned the USA's regulatory framework closer to European standards, particularly in safety assessments, cosmeticovigilance and compliance with GMP. However, the USA remains more flexible, especially for small businesses, with some regulations still under development, such as fragrance labeling and GMP guidelines.

Both regions require some form of registration or notification, but the USA has specific requirements, such as the need for a US agent for foreign companies, whereas the EU mandates an RP within the EU. These differences create challenges for companies to market cosmetics internationally, as they must navigate the distinct regulations in each region. However, the introduction of MoCRA has aligned the USA's regulations more closely with the EU's, particularly in areas such as safety substantiation, registration, and cosmeticovigilance.

For small companies, the implementation of these new requirements under MoCRA could pose significant challenges. These businesses may face increased costs and administrative burdens to meet the new safety and compliance standards. However, despite these challenges, there are also potential opportunities for growth. Companies that are able to meet the new regulatory requirements will be better positioned to build consumer trust, improve product quality, and ultimately differentiate themselves in an increasingly competitive market.

One proposed development of a joint registration strategy for a US-based SME aiming to sell cosmetic products in the EU and US markets involves several crucial steps. The process starts with market analysis and the creation of a “green” product line focused on sustainability and organic ingredients. The strategy includes establishing GMP, TPP, product formulation, packaging design, safety substantiation through CPSR and PIF, cosmeticovigilance system, and a marketing strategy. Implementing this strategy means that small companies will be able to successfully register and sell their cosmetic products in the European and US markets and provide access to new markets and opportunities.

In summary, MoCRA represents a significant step towards improving the quality and safety of cosmetic products for consumers in the USA. By introducing stricter regulations for manufacturing practices, safety evidence, cosmetic monitoring and labeling, MoCRA is intended to improve consumer protection and ensure that cosmetics are safer and more reliable. While it may be difficult for small businesses to comply with the new regulations at first, the long-term benefits of increased consumer confidence and sector growth outweigh the costs and effort.

However, open questions about MoCRA concern the impact on the cosmetics industry, the international harmonization of regulations and the practical implementation. Under MoCRA, the FDA is required to issue final guidelines for GMP. However, it can be assumed that the requirements will be like those of the EU as a global approach takes place. Additionally, under MoCRA, the FDA is tasked with establishing final rules for fragrance allergen labeling, although the exact scope is not yet known. It can, however, be assumed that detailed information on the label will be required to provide consumers with the greatest possible transparency and thus lead to an improvement in safety.

The use of social media channels and advertising has become more important in marketing and advertising and has increased significantly. It is questionable how this should be handled, as there is a possibility that comments under social media posts may contain reports of side effects and need to be monitored.

In the future, promoting transparency and ensuring long-term health impacts will continue to be crucial to focus on, as advancements in scientific research and innovations in cosmetic chemistry play an increasingly important role in shaping the evolution of regulations. These developments will help refine safety standards and regulatory frameworks, ensuring that they align with the latest scientific insights and provide consumers with greater clarity about the products they use, leading to improved quality and safety of cosmetic products.

10.Literature Cited

1. Olson K. Cosmetics in Roman Antiquity: Substance, Remedy, Poison. clw 2009 [cited 2025 Jan 7]; 102(3):291–310. Available from: URL: https://muse.jhu.edu/pub/72/article/266767/pdf.

2. Nayak M, Ligade VS. History of Cosmetic in Egypt, India, and China. J Cosmet Sci 2021; 72(4):432–41.

3. Riesmeier M, Keute J, Veall M-A, Borschneck D, Stevenson A, Garnett A et al. Recipes of Ancient Egyptian kohls more diverse than previously thought. Sci Rep 2022; 12(1):5932.

4. Cleopatra's Eye Makeup Warded Off Infections? 2010 Jan 15 [cited 2025 Jan 7]. Available from: URL: https://www.nationalgeographic.com/science/article/100114-cleopatra-eye-makeup-ancient-egyptians.

5. Victor R. Boswell, JR. Arsenpille & Bleipuder: Die Geschichte des giftigen Make-ups. National Geographic 2019 Dec 3 [cited 2025 Jan 7].

6. Jung EG, Funke J. Kosmetik im Wandel der Jahrtausende [80-92 Seiten / Heidelberger Jahrbücher Online, Bd. 1 (2016): Stabilität im Wandel] 2016 [cited 2025 Jan 12]. Available from: URL: https://www.psychologie.uni-heidelberg.de/ae/allg/mitarb/jf/Jung%20Funke%202016%20Kosmetik.pdf.

7. Cosmetics and Skin: Arsenic-eaters and cucumber creams; 2025 [cited 2025 Jan 11]. Available from: URL: https://www.cosmeticsandskin.com/ded/arsenic.php.

8. U.S Food & Drug Administration. Draft Guidance for Industry: Registration and Listing of Cosmetic Product Facilities and Products [cited 2024 Sep 7]. Available from: URL: https://www.fda.gov/media/170732/download.

9. U.S Food & Drug Administration. Modernization of Cosmetics Regulation Act of 2022 [cited 2024 Dec 29]. Available from: URL: https://www.fda.gov/cosmetics/cosmetics-laws-regulations/modernization-cosmetics-regulation-act-2022?utm_medium=email&utm_source=govdelivery.

10. National Library of Medicine. Images From the History of the Public Health Service: Pure Food and Drugs; 2024 [cited 2024 Nov 30]. Available from: URL: https://www.nlm.nih.gov/exhibition/phs_history/foodanddrugs.html.

11. Riewerts K. Kosmetische Mittel vom Kaiserreich bis zur Zeit der Weimarer Republik [Elektronische Ressource] : Herstellung, Entwicklung und Verbraucherschutz 2005.

12. U.S. Cosmetics Market Size & Share | Industry Report, 2030; 2024 [cited 2024 Nov 28]. Available from: URL: https://www.grandviewresearch.com/industry-analysis/us-cosmetics-market-report.

13. Europa Schönheits- und Körperpflegeprodukte Marktgröße | Mordor Intelligence; 2024 [cited 2024 Nov 29]. Available from: URL: https://www.mordorintelligence.com/de/industry-reports/europe-beauty-and-personal-care-products-market-industry.

14. International Trade Administration | Trade.gov. EU Cosmetics; 2024 [cited 2024 Nov 29]. Available from: URL: https://www.trade.gov/eu-cosmetics.

15. Office P. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products [cited 2024 Aug 10]. Available from: URL: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32009R1223.

16. U.S Food & Drug Administration. Voluntary Cosmetic Registration Program; 2024 [cited 2024 Dec 29]. Available from: URL: https://www.fda.gov/cosmetics/voluntary-cosmetic-registration-program.

17. Micro-, small- and medium-sized enterprises: definition and scope | EUR-Lex; 2025 [cited 2025 Jan 16]. Available from: URL: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=LEGISSUM%3An26026.

18. United States Trade Representative. Small- and Medium-Sized Enterprises (SMEs); 2024 [cited 2024 Dec 28]. Available from: URL: https://ustr.gov/trade-agreements/free-trade-agreements/transatlantic-trade-and-investment-partnership-t-tip/t-tip-12.

19. 13 CFR 121.201 -- What size standards has SBA identified by North American Industry Classification System codes?; 2024 [cited 2024 Dec 28]. Available from: URL: https://www.ecfr.gov/current/title-13/chapter-I/part-121/subpart-A/subject-group-ECFRf12a11421b08a31/section-121.201.

20. Burrows V. A Century of Ensuring Safe Foods and Cosmetics [cited 2024 Nov 30]. Available from: URL: https://www.fda.gov/media/110464/download.

21. Alice T Gasch MD. Lash Lure and Paraphenylenediamine: Toxic Beauty Past and Present: American Academy of Ophthalmology; 2017 [cited 2025 Jan 11]. Available from: URL: https://www.aao.org/lifetime-engaged-ophthalmologist/perspective/article/lash-lure-paraphenylenediamine-toxic-beauty.

22. Cosmetics and Skin: Lash Lure; 2024 [cited 2024 Dec 4]. Available from: URL: https://www.cosmeticsandskin.com/bcb/lash-lure.php.

23. Color Additives and Cosmetics: Fact Sheet. FDA Mon, 2024 Sep 30 [cited 2024 Dec 28]. Available from: URL: https://www.fda.gov/industry/color-additives/color-additives-and-cosmetics-fact-sheet.

24. Summary of Cosmetics Labeling Requirements. FDA Mon, 2024 Sep 30 [cited 2024 Nov 30]. Available from: URL: https://www.fda.gov/cosmetics/cosmetics-labeling-regulations/summary-cosmetics-labeling-requirements.

25. Federal Trade Commission. Fair Packaging and Labeling Act: Regulations Under Section 4 of the Fair Packaging and Labeling Act; 2013 [cited 2024 Nov 30]. Available from: URL: https://www.ftc.gov/legal-library/browse/rules/fair-packaging-labeling-act-regulations-under-section-4-fair-packaging-labeling-act.

26. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364e: Labeling (a) general requirement.

27. U.S Food & Drug Administration. FDA Has Stopped Accepting Submissions to the Voluntary Cosmetic Registration Program (VCRP); 2024 [cited 2024 Feb 10]. Available from: URL: https://www.fda.gov/food/cfsan-constituent-updates/fda-has-stopped-accepting-submissions-voluntary-cosmetic-registration-program-vcrp.

28. Focus Area: Product Safety Surveillance. FDA [cited 2024 Nov 30]. Available from: URL: https://www.fda.gov/science-research/focus-areas-regulatory-science-report/focus-area-product-safety-surveillance.

29. Federal Trade Commission. Advertising and Marketing; 2024 [cited 2024 Nov 30]. Available from: URL: https://www.ftc.gov/business-guidance/advertising-marketing.

30. U.S. Food and Drug Administration. Drug Advertising: A Glossary of Terms. FDA Fri, 2024 Aug 9 [cited 2025 Jan 7]. Available from: URL:

https://www.fda.gov/drugs/prescription-drug-advertising/drug-advertising-glossary-terms#claim.

31. Small Businesses & Homemade Cosmetics: Fact Sheet. FDA Mon, 2024 Sep 30 [cited 2024 Dec 28]. Available from: URL: https://www.fda.gov/cosmetics/resources-industry-cosmetics/small-businesses-homemade-cosmetics-fact-sheet#1.

32. Federal Food, Drug, and Cosmetic Act § 201 (i).

33. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364 Definitions (2) Cosmetic product.

34. Frequently Asked Questions on Soap. FDA Thu, 2024 Aug 22 [cited 2024 Dec 5]. Available from: URL: https://www.fda.gov/cosmetics/cosmetic-products/frequently-asked-questions-soap.

35. Cosmetics & U.S. Law. FDA Thu, 2024 Aug 22 [cited 2024 Nov 30]. Available from: URL: https://www.fda.gov/cosmetics/cosmetics-laws-regulations/cosmetics-us-law.

36. What does FDA regulate?; Fri, 2024 [cited 2024 Nov 30]. Available from: URL: https://www.fda.gov/about-fda/what-we-do/what-does-fda-regulate.

37. Federal Trade Commission. Fair Packaging and Labeling Act; 2013 [cited 2024 Nov 30]. Available from: URL: https://www.ftc.gov/legal-library/browse/statutes/fair-packaging-labeling-act.

38. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364d Safety substantiation (c) Definition (1) Adequate substantiation of safety.

39. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364h: small businesses (a) in general.

40. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364h: small businesses (b) Requirements applicable to all manufacturers and processors of cosmetics.

41. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364 Definitions (4) Responsible person.

42. 16 CFR Part 502 -- Regulations Under Section 5(C) of the Fair Packaging and Labeling Act; 2024 [cited 2024 Dec 29]. Available from: URL: https://www.ecfr.gov/current/title-16/chapter-I/subchapter-E/part-502.

43. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics §364a (a) Serious Adverse event reporting requirements.

44. Peter Barton Hutt et al. Legal Distinction in the United States between a Cosmetic and a Drug: 3 rd Edition. Cosmeceuticals and Active Cosmetics:429–42.

45. Title 21-Food and Drugs Chapter I Subchapter G Part 700 Subpart B § 700.35 Cosmetics containing sunscreen ingredients.

46. U.S Food & Drug Administration (FDA). Is It a Cosmetic, a Drug, or Both? (Or Is It Soap?); Fri, 2024 [cited 2024 Mar 10]. Available from: URL: https://www.fda.gov/cosmetics/cosmetics-laws-regulations/it-cosmetic-drug-or-both-or-it-soap#Good.

47. U.S Food & Drug Administration. Per and Polyfluoroalkyl Substances (PFAS) in Cosmetics. FDA Thu, 2024 Aug 22 [cited 2024 Dec 1]. Available from: URL: https://www.fda.gov/cosmetics/cosmetic-ingredients/and-polyfluoroalkyl-substances-pfas-cosmetics.

48. Elena H. Humphreys, David M. Bearden, Laura Gatz, Lance N. Larson, Jerry H. Yen. Federal Role in Responding to Potential Risks of Per- and Polyfluoroalkyl Substances (PFAS) [cited 2024 Dec 1]. Available from: URL: https://crsreports.congress.gov/product/pdf/R/R45986.

49. U.S. Food and Drug Administration. Color Additives History; 2024 [cited 2024 Dec 1]. Available from: URL: https://www.fda.gov/industry/color-additives/color-additives-history.

50. U.S. Food & Drug Administration, Center for Food Safety and Applied Nutrition, Office of Cosmetics and Colors. Guidance for Industry: Safety of Nanomaterials in Cosmetic Products [cited 2024 Oct 8]. Available from: URL: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-safety-nanomaterials-cosmetic-products.

51. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364d Safety substantiation (a) Substantiation of safety.

52. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364d Safety substantiation (c) Definition (2) Safe.

53. U.S Food & Drug Administration. 2022 Testing of Talc-Containing Cosmetics for Asbestos. FDA Thu, 2024 Aug 22 [cited 2024 Oct 8]. Available from: URL: https://www.fda.gov/cosmetics/cosmetic-ingredients/talc.

54. FDA Proposes Rule to Require Standardized Testing Methods for Detecting and Identifying Asbestos in Talc-Containing Cosmetic Products. FDA Fri, 2024 Dec 27 [cited 2024 Dec 27]. Available from: URL: https://www.fda.gov/news-events/press-announcements/fda-proposes-rule-require-standardized-testing-methods-detecting-and-identifying-asbestos-talc.

55. Food and Drug Administration. Talc; Thu, 2024 [cited 2024 Dec 27]. Available from: URL: https://www.fda.gov/cosmetics/cosmetic-ingredients/talc.

56. U.S Food & Drug Administration. Guidance for Industry Cosmetic Good Manufacturing Practices Draft Guidance [cited 2024 Sep 7]. Available from: URL: https://www.fda.gov/media/86366/download.

57. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364b Good manufacturing practice.

58. U.S Food & Drug Administration. Presentation: Good Manufacturing Practices for Cosmetic Products Listening Session (June 1, 2023) [cited 2024 Feb 24]. Available from: URL: https://www.fda.gov/media/168688/download?attachment.

59. Title 21-Food and Drugs Chapter 9 SUBCHAPTER IV-cosmetics §361 Adulterated cosmetics.

60. Title 21-Food and Drugs Chapter 9 SUBCHAPTER IV-cosmetics §362 misbranded cosmetics.

61. Cosmetics Labeling Guide. FDA Thu, 2024 Aug 22 [cited 2024 Oct 27]. Available from: URL: https://www.fda.gov/cosmetics/cosmetics-labeling-regulations/cosmetics-labeling-guide.

62. Federal Trade Commission. Advertising FAQ's: A Guide for Small Business; 2001 [cited 2024 Nov 28]. Available from: URL: https://www.ftc.gov/business-guidance/resources/advertising-faqs-guide-small-business.

63. Cosmetics Labeling Claims. FDA Thu, 2024 Aug 22 [cited 2024 Nov 28]. Available from: URL: https://www.fda.gov/cosmetics/cosmetics-labeling/cosmetics-labeling-claims.

64. U.S Food & Drug Administration. Be Natural Organics - 523615 - 07/19/2017. FDA Fri, 2024 Aug 9 [cited 2025 Jan 2]. Available from: URL: https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/be-natural-organics-523615-07192017.

65. Skin 2 Spirit - 523208 - 08/10/2017. FDA Fri, 2024 Aug 9 [cited 2025 Jan 2]. Available from: URL: https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/skin-2-spirit-523208-08102017.

66. Modernization of Cosmetics Regulation Act of 2022 (MoCRA). FDA Thu, 2024 Aug 22 [cited 2024 Oct 27]. Available from: URL: https://www.fda.gov/cosmetics/cosmetics-laws-regulations/modernization-cosmetics-regulation-act-2022-mocra.

67. Title 21-Food and Drugs Chapter I SUBCHAPTER G Part 700 Subpart B §700 Tamper-resistant packaging requirements for cosmetic products (b) Requirement for tamper-resistant package.

68. U.S Food & Drug Administration. Cosmetic Labeling Guide [cited 2025 Jan 10]. Available from: URL: https://www.fda.gov/media/88234/download.

69. FDA Announces Launch of Cosmetics Direct for Electronic Registration and Listing of Cosmetic Product Facilities and Products. FDA Thu, 2024 Aug 22 [cited 2024 Dec 1]. Available from: URL: https://www.fda.gov/cosmetics/cosmetics-news-events/fda-announces-launch-cosmetics-direct-electronic-registration-and-listing-cosmetic-product.

70. U.S Food & Drug Administration. Inspection of Cosmetics. FDA Mon, 2022 Mar 14 [cited 2024 Oct 20]. Available from: URL: https://www.fda.gov/cosmetics/cosmetics-compliance-enforcement/inspection-cosmetics.

71. U.S. Food and Drug Administration. FDA Recall Policy for Cosmetics; Fri, 2024 [cited 2024 Oct 4]. Available from: URL: https://www.fda.gov/cosmetics/cosmetics-compliance-enforcement/fda-recall-policy-cosmetics.

72. Vigan M, Castelain F. Cosmetovigilance: definition, regulation and use "in practice". Eur J Dermatol 2014; 24(6):643–9. Available from: URL: https://link.springer.com/article/10.1684/ejd.2014.2493.

73. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364 Definitions (1) Adverse Event.

74. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364 Definitions (5) Serious Adverse Event.

75. Toklu HZ, Antigua A, Lewis V, Reynolds M, Jones J. Cosmetovigilance: A review of the current literature. J Family Med Prim Care 2019 [cited 2025 Jan 8]; 8(5):1540–5. Available from: URL: https://pmc.ncbi.nlm.nih.gov/articles/PMC6559068/pdf/JFMPC-8-1540.pdf.

76. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics §364a (b) Submission of reports.

77. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364a Adverse Event (e) (1) Maintenance.

78. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364a Adverse Event (e) (2) Inspection.

79. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364g: Mandatory recall authority.

80. Federal Food, Drug, and Cosmetic Act § 610 and 704 Records inspection.

81. Title 21-Food and Drugs Chapter 9 SUBCHAPTER II sec 321 Definitions; generally (g) definition of drug.

82. Norm DIN EN ISO 22716 "Kosmetik - Gute Herstellungspraxis (GMP) - Leitfaden zur Guten Herstellungspraxis"; 2024 [cited 2024 Dec 1].

83. Richtlinie - 76/768 - EN - EUR-Lex. Richtlinie - 76/768 - EN - EUR-Lex; 2024 [cited 2024 Sep 28]. Available from: URL: https://eur-lex.europa.eu/legal-content/DE/ALL/?uri=CELEX:31976L0768.

84. 40 Year of EU Cosmetics Legistration [cited 2025 Jan 3]. Available from: URL: https://www.cosmeticseurope.eu/files/3414/7427/6539/40_years_timeline.pdf.

85. 6th Amendment of Council Directive 76/768/EEC: 76/768/EEC; 2025 [cited 2025 Jan 3]. Available from: URL: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A01976L0768-19980918.

86. Office P. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products [cited 2024 Sep 13]. Available from: URL: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32009R1223.

87. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 13 Notification (1) sec (a)-(h).

88. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 18 Animal testing.

89. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 2 definitions 1(a).

90. CPNP – Cosmetic Products Notification Portal; 2024 [cited 2024 Sep 28]. Available from: URL: https://webgate.ec.europa.eu/cpnp/.

91. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products ANNEX II.

92. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products ANNEX III.

93. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products ANNEX I.

94. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 19 Labelling 1 (d).

95. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 19 Labelling 1 (g).

96. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 4 Responsible Person (1).

97. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products ANNEX I Part B.

98. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 11 Product information file (3).

99. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 8 Good Manufacturing Practice.

100. Good Manufacturing Practice (GMP) Guidelines/Inspection Checklist for Cosmetics. FDA Thu, 2022 Mar 3 [cited 2024 Mar 20]. Available from: URL: https://www.fda.gov/cosmetics/cosmetics-guidance-documents/good-manufacturing-practice-gmp-guidelinesinspection-checklist-cosmetics.

101. Martine G. CPNP – Für verantwortliche Personen und Händler.

102. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 5 Obligation of responsible persons (3).

103. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 14 Restrictions for substances listed in the Annexes.

104. Gesetzliche Regelungen bei Inhaltsstoffen; 2024 [cited 2024 Nov 2]. Available from: URL: https://www.bvl.bund.de/DE/Arbeitsbereiche/03_Verbraucherprodukte/03_AntragstellerUnternehmen/02_Kosmetik/04_Inhaltsstoffe/bgs_fuerAntragsteller_kosmetik_gesetzlicheRegelung_inhaltsstoffe_node.html.

105. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products ANNEX IV-VI.

106. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 16 Nanomaterial.

107. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 10 Safety Assessment (1).

108. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 11 Product information file (1).

109. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 10 Safety Assessment (2).

110. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 10 Safety Assessment (3).

111. Internal Market, Industry, Entrepreneurship and SMEs. Ban on animal testing; 2024 [cited 2024 Nov 3]. Available from: URL: https://single-market-economy.ec.europa.eu/sectors/cosmetics/ban-animal-testing_en.

112. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 19 Labelling paragraph 5.

113. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 19 Labelling paragraph 1.

114. Office P. Commission Regulation (EU) No 655/2013 of 10 July 2013 laying down common criteria for the justification of claims used in relation to cosmetic products [cited 2024 Nov 27]. Available from: URL: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32013R0655.

115. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 20 Product claims (1).

116. Agreed by the Sub-Working Group on Claims. Technical document on cosmetic claims; Version of 2017.

117. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 23 Communication of serious undesirable effects (1).

118. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products ANNEX I Part A.

119. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 2 Definitions (r) recall.

120. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 5 Obligation of responsible persons (2).

121. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 5 Obligation of responsible persons.

122. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 25 Non-compliance by the responsible person.

123. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 2 Safeguard clause (1).

124. Office P. DIRECTIVE 2001/83/EC on the community code relating the medicinal products for human use Title I Definition Article 1 sec 2 medicinal product.

125. Office P. REGULATION (EU) No 536/•2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL - of 16 April 2014 - on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC of 16 April 2014 [cited 2024 Dec 1]. Available from: URL: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0536.

126. European Medicines Agency (EMA). Pharmacovigilance: Overview | European Medicines Agency (EMA); 2024 [cited 2024 Dec 1]. Available from: URL: https://www.ema.europa.eu/en/human-regulatory-overview/pharmacovigilance-overview.

127. Opinion on Vitamin A (Retinol, Retinyl Acetate, Retinyl Palmitate) [cited 2024 Dec 3]. Available from: URL: https://health.ec.europa.eu/document/download/f1881bcd-ee58-4d42-9701-3feaaa26de61_en.

128. CosIng - Cosmetics - GROWTH - European Commission HYALURONIC ACID; 2024 [cited 2024 Dec 4]. Available from: URL: https://ec.europa.eu/growth/tools-databases/cosing/details/34315.

129. CosIng - Cosmetics - GROWTH - European Commission Glycerin; 2024 [cited 2024 Dec 3]. Available from: URL: https://ec.europa.eu/growth/tools-databases/cosing/details/34040.

130. CosIng - Cosmetics - GROWTH - European Commission Aloe Vera leaf extract; 2024 [cited 2024 Dec 3]. Available from: URL: https://ec.europa.eu/growth/tools-databases/cosing/details/100295.

131. Title 21-Food and Drugs Chapter I SUBCHAPTER G Part 710 § 710.9 Exemptions.

132. Title 21-Food and Drugs Chapter I SUBCHAPTER G - COSMETICS Part 700 General Subpart B Sec. 700.11 Cosmetics containing bithionol [cited 2024 Oct 6].

133. Title 21-Food and Drugs Chapter I- Subchapter G Part 700 Subpart B §700.13 Use of mercury compounds in cosmetics including use as skinbleaching agents in cosmetic preparations also regarded as drugs. Available from: URL: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=700.

134. Title 21-Food and Drugs Chapter I Subchapter G Part 700 Subpart B § 700.14 Use of vinyl chloride as an ingredient, including propellant of cosmetic aerosol products.

135. Title 21-Food and Drugs Chapter I Subchapter G Part 700 Subpart B § 700.23 Chlorofluorocarbon propellants.

136. Title 21-Food and Drugs Chapter I Subchapter G Part 700 Subpart B § 700.15 Use of certain halogenated salicylanilides as ingredients in cosmetic products.

137. Title 21-Food and Drugs Chapter I Subchapter G Part 700 Subpart B § 700.18 Use of chloroform as an ingredient in cosmetic products.

138. Title 21-Food and Drugs Chapter I Subchapter G Part 700 Subpart B § 700.19 Use of methylene chloride as an ingredient of cosmetic products.: 21 CFR 700.19; Law in effect on 2024.

139. Title 21-Food and Drugs Chapter I Subchapter G Part 700 Subpart B § 700.16 Use of aerosol cosmetic products containing zirconium.

140. Title 21-Food and Drugs Chapter I Subchapter G Part 700 Subpart B § 700.27 Use of prohibited cattle materials in cosmetic products.

141. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364c Registration and product listing (a) Submission of registration.

142. Title 21-Food and Drugs Chapter 9 SUBCHAPTER VI Cosmetics Sec. 364c Registration and product listing (c) Cosmetic product listing.

143. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 11 Product information file (2) Point (a)-(e).

144. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 11 Product information file (2) Point d.

145. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 19 Labelling paragraph 1 point (a).

146. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 19 Labelling Paragraph 1 Section (b).

147. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 19 Labelling paragraph 1 section (c).

148. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 19 Labelling 1 (e).

149. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 19 Labelling 1 (f).

150. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 19 Labelling paragraph 1 point (g).

151. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 19 Labelling paragraph 6.

152. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Article 19 Labelling paragraph 2..

ANNEX I

FDA Registration obligation exception for Cosmetic Products in the USA:

Additionally, in accordance with 21 CFR 710.9 the registration obligation is not applicable for all establishments listed below (131):

- Beauty shops and stores (except if the establishment manufactures or performs cosmetic processing on the premises),
- Retailers of cosmetic products, including individual and direct sales representatives, retail distribution facilities, and pharmacies, apart from those that manufacture or process cosmetic products that are sold directly to consumers at that location,
- Hospitals, medical practices and clinics in the healthcare sector,
- Public health authorities and other non-commercial institutes supply cosmetics to consumer directly,
- Establishments, e.g. hotels and airlines, that offer their customers free cosmetic products in connection with other services,
- Trade fairs and other events at which free samples of cosmetic products are offered.
- An establishment that is engaged in the manufacture or processing of cosmetic products that are used exclusively for use in research or evaluation purposes, including production testing, and are not offered for individual sale,
- An establishment that exclusively carries out one or more of the following activities in relation to cosmetic products, e.g. labeling, relabeling, packaging, repackaging, storage and distribution.

However, this exception does not apply to cosmetic products that regularly are

- in contact with the eye's mucus membrane during customary use, or
- injected, or
- for internal use, or
- designed to alter appearance for over 24 hours without consumer removal as part of normal use.

ANNEX II

FDA List of Prohibited and restricted Ingredients:

Prohibited Ingredients:

- Antibacterial Agents:
  - Bithionol: Antibacterial agent, once used in cosmetics like shampoos and creams, can cause photosensitivity and may trigger cross-sensitivity with other chemicals (132)
- Skin Bleaching Agents:
  - Mercury: commonly used in skin-lightening products, these pose significant health risks (133)
- Aerosol Propellants:
  - Vinyl chloride: Previously used in aerosol cosmetic products, it is now banned due to carcinogenic risks (134)
  - Chlorofluorocarbon (CFC) propellants: Prohibited in pressurized containers for environmental and safety reasons (135)
- Antimicrobial Agent
  - Halogenated Salicylanilides: Used as antimicrobial agents, these are banned due to safety concerns(136)
- Other Hazardous Ingredients:
  - Chloroform: Formerly an ingredient in certain cosmetics, banned due to its toxicity (137)
  - Methylene chloride: Used in aerosol cosmetics, banned due to toxicity (138)
  - Aerosol cosmetics containing zirconium: Ingredient of aerosol anti-perspirants (139)

Restricted Ingredients:

- Animal-derived material: The use of certain cattle material, such as brain or skull tissue is forbidden due to prevent the risk of transmissible diseases (140)

ANNEX III

FDA Mandatory Facility Registration in the USA:

All companies, except for small businesses, must register their facility.

- Any person who owns or operates an existing facility involved in manufacturing or processing cosmetic products for distribution in the USA as of December 29, 2022, is required to register the facility within one year of that date through the Portal Cosmetic Direct System
- Any person who owns or operates a new facility involved in manufacturing or processing cosmetic products for distribution in the United States after December 29, 2022, is required to register the facility within 60 days.
- This includes domestic and foreign facilities. For foreign facilities, the appointment of a U.S. Agent is mandatory to act as a local point of contact for regulatory communications with the FDA.
- The registration must be renewed every two years. All new information must be submitted within 60 days (141).

The registration process for cosmetic facilities under Portal Cosmetics Direct requires specific information

- to be provided in Structured Product Labeling (SPL) format.
    - Including name of the facility
    - Physical address
    - Email address
    - Telephone number.
    - Registration number, if available
    - All brand names under which cosmetic products manufactured or processed at the facility are sold must be listed.

For each cosmetic product, the product category or categories must be specified, along with the identification of the RP associated with the product (141).

FDA Mandatory Cosmetic Product Listing

As already mentioned, all companies, except small businesses, must provide detailed listings of all cosmetic products they market in the USA.

- Each product listing must include:
  - Product name
  - Category or intended use of the product
  - A list of ingredients, including any fragrances, flavors, or colors, with each ingredient identified by their International Nomenclature of cosmetic Ingredients (INCI), names and concentrations (if required)
- Contact data for the RP, as mentioned on the label (142)

ANNEX IV

Content of Product Information File in the EU:

The PIF must contain following information and shall be updated, if it seems required:

- Cosmetic product's description: A detailed description of the product, including its intended use and function (143).
- CPSR: This includes a comprehensive safety assessment of the product, including toxicological profiles of all ingredients, exposure data, and any potential risks associated with the product's use. The CPSR must be based on scientifically robust methods and must be performed by a safety assessor (118).
- Description of the manufacturing process, including a declaration of compliance with cosmetic GMP, such as ISO 22716:2007 or equivalent standards. The process must ensure the product is consistently manufactured to high-quality standards (82).
- Evidence supporting claimed effects were relevant to the nature or effect of the product. Companies must provide evidence that supports the claimed effects. This evidence must be based on scientifically recognized methods or other valid tests (144).
- Data on animal testing: The PIF must document any animal testing conducted by the manufacturer, agents, or suppliers related to the development or safety assessment of the cosmetic product or its ingredients. This includes tests done to meet third-country regulations, although animal testing is prohibited in the EU (143).

Content of the Cosmetic Product Safety Report as a Part of PIF in the EU.

All information listed below are taken from Annex I of 1223/2009 (118)**:**

- **Part A:** Cosmetic product safety information:
  - Of the on the quantitative and qualitative composition product
  - Physical characteristics/ chemical characteristics and stability
  - Microbial quality
  - Impurities, traces and information about packaging material
  - Normal and reasonably foreseeable use
  - Exposure to the cosmetic product: site of application, surface area, amount of applied product, duration and frequency of use, the normal and reasonably foreseeable exposure route(s), targeted (or exposed) population(s). Potential exposure of a specific population shall also be taken into account.
  - Exposure to substances
  - Toxicological profiles of the ingredients
  - All available data on the undesirable effects and serious undesirable effects to the cosmetic product
  - Other relevant information, e.g. existing studies from human volunteers or the duly confirmed and substantiated findings of risk assessments carried out in other relevant areas.

❖ **Part B**: Cosmetic product safety assessment:

- **Assessment conclusion**: Statement on the safety of the cosmetic product

- **Labelled warnings and instructions of use**: Statement on the need to label any particular warnings and instructions of use

- **Reasoning**: Explanation of scientific reasoning leading to the assessment conclusion set out under Section 1 and the statement set out under Section 2. This explanation shall be based on the descriptions set out under Part A. Where relevant, safety margins shall be assessed and discussed.

- **Assessor's credentials and approval of part B**: Name and address of the safety assessor. Proof of qualification of safety assessor. Date and signature of safety assessor.

ANNEX V

Requirement of Cosmetic Product Listing in the EU:

- Name and address of the RP (145),
- Content at the time of packaging, indicated by weight or volume (excepted for small packages under five grams) (146),
- Date of minimum durability, on cosmetics indicating how long the product remains effective under proper storage. It must be marked with a specific symbol or the words “best used before the end of” showing month/year or day/month/year. For products lasting over 30 months, this date is not required; instead, they must show a period-after-opening symbol indicating safe use time after opening (147),
- Origin of product in case of imported product (145),
- Precautions and special safety instruction for products for professional use (94),
- Batch number of manufacturer or any other unique identifier, at least on outer packaging if the product packaging is too small (148),
- Intended use, if not represented by appearance (149),
- If the cosmetic product contain nanomaterial, the term “nano” must be used on the label (150)
- Perfumes and aromatic compositions are listed as "parfum" or "aroma”.
- Colorants, except for hair dyes, may be listed after other ingredients or with "may contain." (150)

Requirement of Labeling in the EU According to Article 19 Labeling of 1229/2009:

- Name and address of the RP (145)
- Must include all substances used in manufacturing, excluding impurities and auxiliary materials absent from the final product.
- List of ingredients: Perfume and aromatic compositions and their raw materials shall be referred to by the terms “parfum” or “aroma”. The list of ingredients must be arranged in descending order of weight at the time they are added to the cosmetic product. Ingredients with concentrations of less than 1% can be listed in any order after those with higher concentrations (95).

- Ingredients should be listed by descending weight, with those under 1 % appearing last, using the common ingredient name. If no common name is available, a term from a widely accepted nomenclature should be used (150, 151).
- If the labeling information as mentioned above is impractical to label, it should be provided on an attached leaflet, label, tape, tag, or card. Where possible, abbreviated information or symbols can be used (152).
- The abbreviation of the responsible person's name and address, as long as it allows identification (145)
- Address where responsible person makes the product information file available (145)
- Origin country, in case of imported cosmetic products (145)
- Content per weigh or volume (146)
- “Date of minimum durability” in MM/YYYY or DD/MM/YYYY (147)
- Mentioning of “nano” (95)
- Batch number (94, 148)

ANNEX VI

EU needed information for the CPNP

The RP shall submit the following information to the EC via CPNP. Specific product information, e.g., name(s) and category

- Responsible person's name and address, including the location of the product file
- Origin country, in case of import
- MS where the cosmetic product will be marketed
- Contact details of a natural person, this person must be able to reach in case of need, e.g. in case of safety concern or consumer complaints
- Nanomaterials, if applicable: the notification must specify the nanomaterial used, including the IUPAC chemical name and the exposure circumstances that can be considered foreseeable (106).
- Carcinogenic, mutagenic, or toxic substances. The name and Chemical Abstracts Service number or IUPAC number of any substances classified as carcinogenic, mutagenic, or toxic for reproduction category 1A or 1B under Annex VI Part 3 of Regulation (EC) No 1272/2008 must be included (105);

  Frame formulation, that allows quick and effective medical treatment in case of complications, e.g. undesirable effects (87)

Erklärung

Hiermit erkläre ich an Eides statt, die Arbeit selbständig verfasst und keine anderen als die angegebenen Hilfsmittel verwendet zu haben.

Köln, 2 February 2025

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K. Grundke