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Review Article

COMPREHENSIVE REGULATIONS FOR DRUG AND COSMETICS IN EUROPEAN UNION

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ABSTRACT

Pharmaceuticals are regulated for quality, safety, and effectiveness by regulators for marketing approval with regard to good manufacturing practices, formulation, labelling, packaging, documentation and qualified individuals. Cosmetics for oneself or others are growing in popularity. The European Union (EU) Cosmetics Directive No. 1223/2009 enforces guidelines for cosmetic preparations. By considering the long-term risks of nanoparticles if misused by researchers and testers, the risk assessment outlined in Article 16 of the cosmetic code provides a framework for increasing the possibilities for innovation in nano-products. On March 14, 2024, the EU Commission published Regulation (EU) 2024/858, amending Cosmetics Regulation European Commission (EC) No. 1223/2009, which updated Annexes II and III regarding the use of certain nanomaterials in cosmetic products. Substances added in Annex II are prohibited from use, whereas those added in Annex III can be used when prescribed restrictions are met like essential conditions under European regulations for the import and sale of cosmetics. In the EU, the manufacturer is responsible for the safety of its products and must ensure that they undergo an expert scientific safety assessment before they are sold. The European Commission is also advised on issues related to the safety and allergenic properties of cosmetic products and ingredients by the Scientific Committee on Consumer Safety (SCCS), administered by the Directorate-General for Health and Food Safety (DG SANTE), informed by independent scientific expertise.

Keywords: Regulations for drugs and cosmetics, Good manufacturing practices, Qualified persons, Artificial intelligence in cosmetics, Nanomaterials in cosmetics

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INTRODUCTION

The regulation of medicinal products and cosmetics plays crucial role in ensuring public health and safety. As per European Union (EU) medicinal products are defined as "a substance or combination of substances that is intended to treat, prevent, or diagnose a disease, or to restore, correct, or modify physiological functions by exerting a pharmacological, immunological, or metabolic action". The European Union (EU) established in the year 1993 has expanded from six to 27 member states, despite challenges like Brexit. It plays a vital role in promoting peace, democracy, and economic integration across Europe. Within the EU's framework, several important organizations help regulate and manage healthcare and medicines. These include the Committee for Medicinal Products for Human Use (CHMP), which reviews and approves medicines for people, and the Pharmacovigilance Risk Assessment Committee (PRAC), which monitors the safety of medicines after they are on the market. The Committee for Medicinal Products for Veterinary Use (CVMP) ensures medicines for animals are safe and effective, while the Committee for Orphan Medicinal Products (COMP) helps support the development of treatments for rare diseases. To streamline the regulatory landscape, the EU has organized its pharmaceutical guidelines into ten volumes that cover laws, manufacturing standards, pharmacovigilance, clinical trials, and more. These volumes ensure the safety, quality, and consistency of medicinal products at every stage from development approval to post-market surveillance. Cosmetics are regulated under (EC) No 1223/2009, which ensures that cosmetic products are safe, properly labelled, and do not pose risks to human health [1].

The EudraLex guidelines, particularly Volume 4, outline Good Manufacturing Practices (GMP), emphasizing labelling, which must include mandatory information such as the marketing authorization number and comply with specific articles to ensure clarity. Packaging requirements mandate that each product contains a package leaflet that is clear and accessible to patients, while variations to approved products must follow specific procedures to ensure ongoing compliance. Each manufacturing authorization holder must have a Qualified Person (QP) responsible for ensuring that products meet all regulatory standards and guidelines. Cosmetics are regulated under Regulation (EC) No. 1223/2009. Furthermore, the EU AI Act addresses the use of Artificial Intelligence (AI) in cosmetics, categorizing AI systems based on risk and establishing varying regulatory requirements. AI offers significant advantages, such as developing personalized skincare products and creating sustainable packaging solutions. This article explores key aspects of EU regulations concerning pharmaceuticals and cosmetics, focusing on safety, compliance, and the integration of artificial intelligence.

Guidelines for pharmaceuticals in EU

The European Medicines Agency (EMA) gives guidelines for human products and veterinary products in its directives, which are in accordance with International Conference for Harmonisation (ICH) guidelines [2]. They are elaborated in the form of volumes; volume 4 is concerned with GMP requirements which are discussed elaborately in the article.

Volume 1: European Union pharmaceutical laws related to medicinal products for human use

Volume 2: Notification to applicants and regulatory guidelines for medicinal products for human use

Volume 3: Scientific guidelines for medicinal products for human use

Volume 4: Guidelines for good manufacturing practices for medicinal products for human and veterinary use

Volume 5: European Union pharmaceutical regulations for medicinal products for veterinary use

Volume 6: Notice to applicants and regulatory guidelines for medicinal products for veterinary use

Volume 7: Scientific guidelines for medicinal products for veterinary use

Volume 8: Maximum residue limits

Volume 9: Pharmacovigilance Guidelines for medicinal products for human and veterinary use

Volume 10: Clinical trial guidelines

Volume 4 Good Manufacturing practices guidelines for medicinal products for human and veterinary use

Volume 4 consist of the principles and guidelines of good manufacturing practices for medicinal products for human and veterinary use are guide by volume 4 European Union, usually laid down in Commission Directives 91/356/EEC (European Economic Community)(veterinary use), and amended by Directive 2003/94/EC (medicinal products for human use) [3]. The European Union's Volume 4 is divided into four sections table 1. lists these sections, each of which addresses a distinct area of pharmaceutical products.

Table 1: Parts of the European Union (EU) GMP guidelines volume 4

Part 1	Basic Requirements for Medicinal Products
Part 2	Basic Requirements for Active Substances used as Starting Materials
Part 3	GMP related documents
Part 4	GMP requirements for Advanced Therapy Medicinal Products

Part 1: Basic requirements for medicinal products: There are nine chapters in Part 1.

Chapter 1: Pharmaceutical Quality System

GMP and quality risk management are the part of pharmaceutical quality system (PQS), which ensures consistency in product delivery. PQS must and should ensure product realization, product and process knowledge management, design and development of Medicinal products, production and control operations, managerial responsibilities, material management, Storage and distribution, Continuous improvement, root cause analysis, Self-inspection and quality audits. Root cause analysis identifies non-conformities, issues that eliminate the problem from recurring permanently by finding a proper solution. Chapter 1 has been amended to align with the ICH Q10 Pharmaceutical Quality System guideline and revised for interpretation of principles and guidelines of GMP in Directive 2003/94/EC for medicinal products in human use and Directive 91/412/EEC for veterinary use [3].

Chapter 2: Personnel

There should be adequately qualified personnel with clearly defined responsibilities. An organizational chart indicating the hierarchy and clear job descriptions should be maintained. It has been revised and new section addresses the role of consultants in accordance with Article 47 of Directive 2001/83/EC for human products and Article 51 of Directive 2001/82/EC for veterinary products [4].

Chapter 3: Premise and equipment

Premises and equipment need to be constructed to prevent cross-contamination, and they must be maintained and calibrated. It has been updated to enhance guidance on preventing cross-contamination, with references to Chapter 5. It also provides guidance on GMP principles as outlined in Directive 2003/94/EC and 91/412/EEC [5].

Chapter 4: Documentation

Should be well-designed, reviewed, approved, and clear. After expiry of the product, records must be stored for at least one year. Revisions address the increasing use of electronic documents in GMP for improved control and retention [6].

Chapter 5: Production

The production department should be compete in supervision, written procedures should be followed, and report any quality issues to quality control department. There should be a quarantine area, maintain the storage conditions properly, yields should be cross-checked. This chapter has been updated to enhance cross-contamination prevention and include toxicological assessments in Sections 17–21. Sections 27–30 focus on supplier qualification and GMP compliance for supply chain traceability. Sections 35 and 36 clarify testing expectations for starting materials, while Section 71 provides guidance on notifying supply restrictions [7].

Chapter 6: Quality control

Must adhere to GMP. Testing methods should be validated, and stability monitored throughout the product's shelf life. A new section on the technical transfer of testing methods has been introduced [8].

Chapter 7: Outsourced activities

Must coordinate with regulations and marketing authorizations. Contract givers should oversee and monitor the outsourced activities, while contract acceptors must maintain suitable facilities and avoid subcontracting without approval**.** It has been revised per ICH Q10 to extend guidance on outsourced GMP-regulated activities beyond contract manufacturing and analysis, with a title change reflecting this expanded scope [9].

Chapter 8: Complaints and product recall

Consist of handling complaints, investigating defects, assessing risks, and implementing corrective actions. Root cause analysis should be thorough, and corrective actions should be monitored for effectiveness. This chapter has been revised to emphasize the application of Quality Risk Management (QRM) principles in investigating quality defects, complaints, and decisions on recalls or risk mitigation. It focuses on identifying root causes, implementing preventive actions, and clarifying responsibilities for reporting defects to Competent Authorities [10].

Chapter 9: Self-inspection

Is carried to ensure GMP compliance and self-inspections are carried out and conducted by competent individuals [11].

Part 2: **Basic requirements for active substances used as starting materials**

This part deals with the production of active substances, which are used as starting materials for medicinal products. It covers the entire process, from the raw materials to the finished active substance. Quality management system includes personnel, buildings, facilities, documentation and records, materials management, production and in-process controls, packaging and identification, storage and distribution, laboratory controls, validation, change control, complaints and recalls, internal audits, must ensure that active substances are consistently produced in accordance with quality standards [12].

Part 3: GMP related documents

Documents include Site Master File (SMF), Quality Risk Management, Q10, Mutual Recognition Agreements (MRA) Batch Certificate, Template for the "written confirmation" for active substances exported to the European Union for medicinal products for human use.

The main goal of SMF is to document quality management policies and site operations. The format of SMF should be 25-30 pages with appendices, use A4 paper, and use simple plans or schematics, layouts, and drawings, must be updated on a regular basis and provide an edition number, effective date, and review date [13]. Q9, Quality Risk Management consists of tools and concepts of quality risk management and is followed throughout the lifecycle of the product [14]. Q10, Note for Guidance on Pharmaceutical Quality System, refers to the systems that support the development and manufacture of pharmaceutical drugs, as well as biotechnology and biological products, throughout the product lifecycle [15]. Mutual Recognition Agreements (MRA) Batch Certificate includes name of the product, address of manufacturing and quality control sites

(name, address, authorization number), importing country, marketing authorization, strength and potency, dosage form, package type and size, batch type, manufacture and expiry dates, GMP compliance certificate, expiry dates, analysis results [16]. Template for the "written confirmation" for active substances exported to the European Union for medicinal products for human use, serves as a written confirmation that the active substance(s) listed below must adhere to Good Manufacturing Practice (GMP) standards that are equivalent to those of the European Union and be routinely inspected by competent authority to ensure ongoing compliance with GMP. It contains the name, address, and contact information of the manufacturer, the competent authority, and the active substance [17].

Part IV-GMP requirements for advanced therapy medicinal products (ATMP)

ATMPs including gene therapy, somatic cell therapy, and tissue-engineered products-demand strict GMP guidelines due to their complexity and associated risks. GMP guidelines for ATMPs adhere to EU regulations set by the European Medicines Agency (EMA) to ensure product safety, quality, and efficacy [18].

Labelling and packaging

The text of the labelling must and should follow articles. Article 9(4) (d) instructs the draft labelling text, Article 54 files the required particulars for packaging, and Article 61(2) makes sure to comply with labelling and characteristics of the product. Article 63(3) talks about the exemptions from labelling requirements under certain conditions, which are desired from European Medicine Agency (EMA). Member States sometimes may ask for further additional labelling information or optional information as initiated by the applicant. The language of the labelling must be in the official language of the member state where the product is to be sold. There are some exemptions where they can be requested for orphan medicinal products under certain conditions. Some members may need additional labelling information, for example, on price, reimbursement, supply, etc. that additional information must be provided in a single blue box on the packaging. Member states may request the legal supply status information on the label, and it must coordinate with the Commission decision. The marketing authorisation number (e. g., "EU/1/96/000/000") must appear on the package, with national identification numbers in the 'blue box'. Optional information includes symbols and pictograms, which give clarity about the information; they should align with product characteristics mentioned in the blue box. Labelling must comply with the Directive, and it will be reviewed by the CHMP and EMA. Mock-ups and specimens are reviewed during the application process. If there are any changes regarding the summary of characteristics of the product, need to be submitted to authority, and they have 90 days to raise the opposition.

Package leaflet for medicinal products

Every product must consist of the package leaflet, which contains information about the product. And it should align with Title V of Directive 2001/83/EC and the product's summary of characteristics. The leaflet must be clear, legible, and easy to use by the patients. The leaflet must be in an official language of the Member State where the product is sold, but it can be printed in multiple languages if the information is identical and legible. Optional information like symbols, pictograms, and additional non-promotional information useful to patients; must be discussed with European Medicine Agency (EMA). Local representatives contact may be present in the leaflet, and it is not compulsory to provide such details. If needed, multiple representatives can also be listed if they do not confuse patients. For blind and partially sighted patients' other formats can be used upon request. The package leaflet must comply with Directive 2001/83/EC. Mock-ups and specimens are checked for readability. And reviewed by CHMP. If there are any changes regarding the leaflet, they must be submitted to the EMA or national authorities. And changes related to the summary of product characteristics follow a particular procedure [19].

EU variations

Modifications to the approved dossier's documents constitute a variation to the terms of a marketing license. Types of variation and details regarding variations are given in table 2.

Table 2: Variations within the European Union are listed

Change or variation	EU-EMA	Impact on quality, safety, efficacy	Anticipated implementation timeline	Guideline approval timeline	Formulation composition change	Manufacturing process change	Equipment change	Reference
Admin	Type 1A	No impact on quality and performance	EU: up to 1 y before submission	EU: N/A(Not Applicable)	Partial deletion of colour, flavour	Minor addition or deletion of a code imprint by embossing, debossing, engraving	Changes from no automated-to-automated equipment to move ingredients	[20]
Minor	Type $1A_{IN}$	Minor changes. Unlikely to have impact on quality and performance	EU: 14 d before submission	EU: N/A	Change in excipient NMT (Not More Than)5%	Changes in timing, operating speeds with application validation changes	Changes to alternative equipment of the same design and same principles	[20]
Moderate	Type 1B	Moderate changes could have impact on quality and performance	EU: 3 mo after submission	EU: 30 d	Change in technical grade of excipient NMT 10%	Any changes outside of applicator validation ranges	-	[20]
Major	Type II	Major changes. likely to have impact on quality and performance	EU: 3 mo after submission	EU: 60 d	Quantitative and Qualitative changes in formulation beyond level 1	Any changes in process such as wet granulator to direct compression	Changes in equipment to a different design and different operating principles	[20]

Qualified person (QP) in European Union

In Article 48, the Directive 2001/83 requests that EU Member States have to assure that each holder of a manufacturing authorization has to have at least one QP. Many importers are hesitant to take at the function of Responsible Person because of its stringent necessities and massive felony responsibilities. This function needs tremendous qualifications and a radical expertise of EU regulations. According to Directive 2001/83, article 49 the educational specifications of qualified person shall complete a Diploma course or bachelor's degree of at least 4 y including theory and practical study of the following subjects: pharmacy, medicine, veterinary medicine, chemistry, pharmaceutical chemistry and technology, biology and shall have practical experience of minimum 2 y [21].

Role/responsibilities of qualified person (QP)

Production department head responsibilities include to ensure produced and stored products according to documentation of quality requirements, assure the production department that the appropriate validations are done, to make sure that the specified preliminary and continuing training of his department personnel is achieved and tailored in keeping with need. Quality control head responsibilities involve approving or rejecting materials from initial

to final making sure data is examined, to approve sampling instructions, check techniques and different Quality Control tactics [22]. Certification of batch release within the European Union (EU) of medicinal products for human or veterinary use holding a Marketing Authorization (MA) or made for export, which applies for Investigational Medicinal Products (IMP) for human use. To ensure the overall safety, quality and efficacy with respect to the Marketing Authorization Holder (MAH). QP verifies each batch in respective with GMP and MA. Batch release process involves verification of manufacturing and testing the batch release methods, certification and transportation of finished products by QP in compliance with quality.

Certification process

Each batch which is going for export and import should be certified by QP within EU, of a manufacturer which are mentioned in MA. QP should acquire knowledge for certification in the areas of overall steps of batch manufacturing to MA and finished product must ensure the steps which have been completed under accepted pharmaceutical quality systems to assure compliance of the batch with GMP, the MA and any other legal obligations in the Member State where certification is taking place. Different imported finished product batches may originate from the same bulk product batch. Qualified Persons (QPs) certifying these distinct batches can base their decisions on the quality control testing of the primary imported batch, provided a justification is documented based on quality risk management principles. Evidence must be documented to establish the integrity and identity of the finished product batch, including compliance with storage requirements for the bulk product prior to packaging; proper storage and transportation conditions; stability of the consignment with no evidence of tampering; correct identification of the product; and representative sampling from all finished product batches derived from the bulk batch. The QP must personally ensure that the following operational responsibilities are fulfilled prior to certification of a batch for release to market or for export. Certification is permitted under the terms of the MA, any additional duties and requirements of national legislation are complied with, certification is recorded in a register or equivalent document [23]. In few cases, the QP will rely on the correct functioning of the pharmaceutical quality system of product manufacturing sites and, which may be derived from audits associated with third parties. The Qualified Person (QP) must verify that the requirements for active substances, packaging materials, excipients, and medicinal products are met, investigating any deviations and correcting their root causes. The impact of deviations should be assessed through a quality risk management process, evaluating their potential effects on the batch's quality, safety, or efficacy and determining whether affected batches should be included in the stability program. Medicinal product batches can only be released for sale after QP certification; until then, they must remain at the manufacturing site or be quarantined at an approved location. Safeguards must prevent uncertified batches from entering saleable stock, and procedures for notifying QP certification to receiving sites must be documented in a technical agreement.

Cosmetics regulation

The EU now regulates the composition, labelling, and packaging of cosmetic items through the Cosmetics Regulation (1223/2009), which was published on July 11, 2013, completely replacing the Cosmetics Directive (76/768/EC). The Common Criteria Regulation (655/2013), which established standards for substantiating claims made for cosmetic products under Article 20(2) of the Cosmetics Regulation, consist of the chapters, articles, topics. Table 3 details about those chapters, articles, topics.

Table 3: Information on chapters articles of cosmetic regulations in EU

Chapters	Articles	Topic	Reference
1	1-2	Scope, Definitions	[24]
2	3-9	Safety, Responsible Person, Obligations of responsible persons, Obligations of distributors, Identification within the supply chain, good manufacturing practice, Free movement	[24]
3	10-13	Safety assessment, Product Information file, sampling and analysis, notification.	[24]
4	14-17	Restrictions for substances listed in the Annexes, Substances classified as Carcinogenic, Mutagenic or toxic for Reproduction (CMR) substances, Nanomaterials, Traces of prohibited substances	[24]
5	18	Animal testing	[24]
6	19-21	Labelling, Product claims, Access to information for the public	[24]
7	22-24	Restrictions for substances listed in the Annexes, Substances classified as CMR substances, Nanomaterials, Traces of prohibited substances	[24]
8	25-28	Animal testing	[24]
9	29-30	Labelling, Product claims, Access to information for the public	[24]
10	31-40	Amendment of the Annexes, Committee procedure, Glossary of common ingredient names, Competent authorities, poison control centres or assimilated entities, Annual report on animal testing, Formal objection against harmonised standards, Penalties, Repeal, Transitional provisions, Entry into force and date of application.	[24]

The most significant change introduced by the cosmetics regulation include safety regulations for cosmetic products; responsible individuals central notice (via Cosmetic Products Notification Portal (CPNP)) of all cosmetics goods introduced on the EU market, reporting of major unfavourable effects, new regulations, such as those pertaining to nanomaterials in cosmetics. The rules governing cosmetic products in the European Union include three volumes. Volume 1 is cosmetics legislation and cosmetic products, volume 2 methods of analysis of cosmetic products, volume 3 outlines the guidelines of cosmetic products. "A cornerstone of the European union, cosmetics marketing is called a single market within the member states of the European union". They are how to make the products, developing the cosmetics, reaching the product.

Manufacture of cosmetics in European Union: (International standard organisation (ISO) 22716)

To guarantee product quality, ISO 22716 offers recommendations for Good Manufacturing Practices (GMP) in the cosmetics sector. These rules encompass manufacturing, control, and shipment. The qualified workforce with good cleanliness and frequent training are important components. The premises must be tidy and well-organised. Equipment needs to be appropriate, sanitised, cleanable, and well-maintained. Packaging and raw materials need to fulfil quality standards. Finished products must meet acceptance criteria and be handled, stored, and sent correctly. In addition to managing results that don't meet specifications, the quality control lab must ensure sampling, testing, and release. Subcontracting agreements should guarantee adherence to GMP specifications, deviations must be backed up by enough facts, and remedial action must be done to stop the recurrence of the deviation. Corrective steps are taken after managing complaints and recalls. Processes and documentation in hard copy or electronic form are maintained [25].

Cosmetovigilance

Serious undesirable effects of cosmetics must be reported to the responsible person and relevant authorities to ensure safety across the EU. When users or health professionals report these effects, the competent authority must inform the responsible person.

Companies and authorities involved in manufacturing must comply with Good Manufacturing Practices (GMP) and conduct physical inspections and laboratory tests. Member states are required to perform regular market surveillance and conduct a comprehensive review every four years [25].

Requirements for importing the cosmetics in EU include compliance with regulation (EC) No 1223/2009, Product Information File (PIF), responsible person, CPNP, labelling requirements, GMP, substance Restrictions, and market surveillance. To sell cosmetics in EU, safety assessment should be conducted by qualified assessor to ensure it is safe to use under normal condition, product information file for each cosmetic product, containing details on composition, safety assessments, and manufacturing information are required. Responsible person or QP must ensure compliance with European Union regulations and acts as contact for authorities. The cosmetic product should be registered with the CPNP, and labelling must meet EU requirements [25].

Artifical intelligence on cosmetic regulation

The European Union's approach to Artificial Intelligence (AI) emphasizes excellence and trust while safeguarding individual rights. This is encapsulated in the EU AI Act, the first regulation on AI, introduced in April 2021. The Act establishes a framework for analysing and classifying AI systems based on their risk levels, which will dictate the regulatory measures needed for their use [26]. AI types in cosmetics is given in table 4.

AI legislation includes varying regulations with regard to transparency and supporting innovation based on risk levels, unacceptable risk and high risk.

AI enhances the EU cosmetics industry by, creating personalized skincare solutions tailored to individual needs, optimizing sustainable packaging to minimize waste, discovering new cosmetic ingredients at the molecular level, reducing biases in AI for fair applications and analysing consumer data to forecast trends and demand [26].

Table 4: AI (Artificial intelligence) types in cosmetics

Type	Description	References
Facial recognition technology (deep learning)	Analyse complex data for virtual try-on applications.	[26]
Machine learning	Provide personalized product recommendations by identifying patterns and making predictions.	[26]
Natural language processing	Powers chatbots to understand and respond to customer inquiries. Analyzes ingredient labels and safety documentation.	[26]

Methods of AI for saftey testing: in silico testing

In silico toxicology predicts specific hazards using computational models, gaining importance in the cosmetics industry due to bans on animal testing.

A. QSAR Models: Quantitative Structure-Activity Relationship (QSAR) models predict the physicochemical, biological, and environmental properties of compounds based on their chemical structure. These models use qualitative Structure-Activity Relationship (SAR) and quantitative data to relate chemical structure to specific properties or activities [26].

B. Read Across: This method infers the properties of new materials based on similarities to known substances. It aligns with the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Regulation, which addresses substance properties, exposure, uses, and risk management [27].

C. Adverse Outcome Pathway (AOP) Modelling: AOPs outline a series of biological events leading to adverse health effects from exposure to a stressor (e. g., a chemical). Researchers develop AOPs for risk assessment and regulatory decision-making, using New Approach Methodologies (NAMs) to evaluate ecological risks [27].

Skin stimulation

It may be regulated to make sure purchaser protection and product efficacy as in keeping with the REACH regulation

A. VIRTUAL SKIN MODELS: Virtual skin models are advanced tools in the cosmetics industry, allowing the simulation of human skin reactions without animal testing. Created using 3D printing, electrospinning and microfluidic structures, these models facilitate controlled, ethical, and cost-effective testing of cosmetic products. Developing a digital skin twin involves complex calculations across various variables and includes modules for data collection, structure library, model generation, simulations, and predictions of diffusivity, partition coefficient, and permeability.

B. IMAGE ANALYSIS: Image evaluation is a powerful tool in the cosmetics industry that uses advanced imaging technology to assess skin properties such as wrinkles, discoloration, and texture. This process helps quantify product effectiveness and ensures that cosmetics meet consumer expectations.

Ingredient screening

Aspect screening in cosmetics inside EU entails in step with identity of ingredients, protection evaluation, compliance with reach and Scientific Committee on Consumer Safety (SCCS) [28].

A. Database mining

B. Risk assessment

Nanomaterials in cosmetics

Article 2(1) of the EU Cosmetics Regulation defines a nanomaterial as a synthetic substance with dimensions ranging from 1 to 100 nm. In March 2024, Regulation (EU) 2024/858 amended this regulation, updating Annexes II and III to prohibit certain nanomaterials while allowing others under specific restrictions. This framework ensures the safety and efficacy of cosmetic products containing nanomaterials, balancing innovation with consumer protection, REACH regulation applies the latter definition. This distinction can create discrepancies, a cloth is probably categorized as a nanomaterial in keeping with the REACH Regulation, however now no longer under the EU Cosmetics Regulation [28].

The SCCS has identified nanomaterials as a critical issue in the EU cosmetics industry. On March 8, 2021, the SCCS published a corrigendum to its earlier recommendations regarding the safety of nanomaterials in cosmetics, initially released on January 8, 2021. The committee also issued preliminary opinions on several specific nanomaterials, including Gold (nano) and Colloidal Gold (nano). According to Article 16 of the EU Cosmetics Regulation, cosmetic products containing nanomaterials must be notified to the European Commission at least six months before being marketed. If safety concerns arise, the Commission must consult the SCCS. The EU Commission maintains and annually updates a list of nanomaterials used in cosmetic products based on data submitted through the CPNP [28].

The SCCS's recommendations for nanomaterial safety in cosmetics highlight several key risk factors:

- **Particle size:** Smaller particles (under 100 nm) may penetrate biological barriers, increasing potential harm.

- **Morphology:** Unique shapes, like needle-like structures, can pose greater toxicity risks.

- **Biokinetics:** Nanomaterials behave differently in the body than bulk materials, affecting their safety.

- **Accumulation:** Evidence of nanoparticle accumulation in tissues raises health concerns.

- **Inhalable products:** Products containing inhalable nanomaterials pose higher respiratory risks.

These assessments aim to ensure consumer protection while allowing innovation in cosmetic formulations. Notifications to the CPNP offer crucial insights into the EU cosmetics market, indicating that while the use of nanomaterials is increasing, it still makes up a minor portion of the overall market. Approximately 800 new cosmetics are notified daily, with only around 10 featuring nanomaterials. In 2020, there were 3,444 notifications under Article 13 and 137 under Article 16, highlighting that most cosmetics containing nanomaterials utilize them primarily as colorants or UV filters. This suggests a cautious approach to incorporating nanomaterials in cosmetic products, reflecting ongoing regulatory scrutiny.

CONCLUSION

This regulatory framework for drugs and cosmetics has been thoroughly covered in this article, which includes important guidance documents, GMP, the role of the QP, Annex 16 for drugs, and various aspects of market operations, including surveillance, imports, sales, distribution. These regulations ensure that products meet the highest safety, quality, and efficacy standards, benefiting both consumers and the industry. However, navigating this complex regulatory landscape presents challenges for manufacturers. To operate efficiently, collaboration between regulators, manufacturers, and stakeholders is essential. Implementing digital tools for regulatory compliance, fostering transparency in supply chains, and harmonizing guidelines with global standards could further streamline processes. Moreover, regulators should focus on continuous improvement by responding to industry innovations—such as advanced therapies and sustainable cosmetic practices with flexible, adaptive frameworks. By adopting these strategies, manufacturers can ensure compliance, drive innovation, and compete effectively. Understanding these regulations enables smooth market entry while safeguarding public health and consumer safety.

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Prasanthi D.: Planned and designed the concept of the manuscript, reviewing the manuscript, designing the final version to be published.

Radhika G.: Supported in designing, drafting the manuscript, literature search and review.

Sharvani A.: Supported in designing, literature search, review, drafting the manuscript.

Hemanth Eswar Teja Y.: Supported literature search and review.

CONFLICT OF INTERESTS

Declared none

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