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Review

Nanomaterials in Cosmetics: An Outlook for European Regulatory Requirements and a Step Forward in Sustainability

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Abstract: The use of materials and products that improve appearance and provide comfort and well-being goes back to the beginning of civilization. Cosmetics is an evolving market that has increasingly focused on innovative technological approaches. Nanotechnology is one of the most revolutionary and promising fields for the development of novel and enhanced cosmetic products, owing to the remarkable multifunctional characteristics and effects of nanomaterials (NMs). Their application, however, also raises potential safety concerns. Some of these concerns can be addressed by determining the type of NMs used, as well as their stability, potential for skin absorption, route of exposure, and how they are formulated into cosmetic products. To guarantee such safety, cosmetic products containing NMs, must comply with European regulatory provisions, particularly the European Regulation (EC) n.° 1223/2009 of the European Parliament and of the Council. Hence, this review comprises all the particularities of NMs, their influence on human health, challenges towards environmental sustainability, and strategies to harmonize policies with the aim to normalize their application in cosmetics.

Keywords: nanomaterial; nanotechnology; regulation; European Union

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1. Introduction

Nanotechnology is a revolutionary and promising field that has recently seen significant advancements and widespread use in cosmetics, dermatology, and biological applications. The size of nanoparticles (NPs) varies between 1 and 100 nanometers. Invisible by the human eye, NPs can present significantly different physical and chemical properties, which are able to provide cleaner, lighter, stronger, and "smarter" surfaces and structures. Scientists have created novel technologies and delivery systems that are being used in the production of cosmeceuticals [1].

Compared with micro-scale cosmetics, nanomaterial-based cosmetics present unique attributes. Nanomaterials (NMs) have a larger contact surface, allowing for longer-lasting

and more efficient effects. Their use is already widespread and can be commonly found in sunscreens, where they assume the function of making the product optically transparent as well as providing protection against solar radiation, or in cosmetic products, such as make-up with long-lasting color effect [2]. Although there are technical and economic benefits to the use of nanotechnology in cosmetics, there are also concerns regarding serious hazards to consumer health and safety [3]. In this sense, it is necessary to follow the regulatory framework that governs nano-enhanced products and ensure that their requirements are monitored by the authorities and complied with by the industry [4].

2. Regulatory Framework of Cosmetics (An Overview)

European Regulation (EC) n.° 1223/2009 of the European Parliament and of the Council (hereinafter referred to as Regulation (EC) n.° 1223/2009 establishes rules to be complied with by any cosmetic product made available on the European Union (EU) market in order to ensure the functioning of the internal market and a high level of protection of human health. In this regulation, a cosmetic is defined as "any substance or mixture intended to be brought into contact with the external parts of the human body (epidermis, hair and capillary systems, nails, lips and external genitalia) or with the teeth and oral mucosa, with a view, exclusively or mainly, to cleaning them, perfuming them, modifying their appearance, protecting them, keeping them in good condition or correcting the body odors" [5].

The Council Directive 76/768/EEC of 27 July 1976, arose from a need to approximate the laws of the Member States (MSs) relating to cosmetic products in order to enable the free circulation of cosmetic products within the EU with harmonized labelling, packaging, and safety regulations. The directive provided the European cosmetics sector with the first safety and quality guidelines. The directive was subsequently repealed by the European Community, and the Regulation of the European Commission (EC) n.° 1223/2009 was published by the European Parliament and the Council in November 2009. The Regulation (EC) n.° 1223/2009 constitutes the legal framework of all cosmetic products produced or/and commercialized in the EU [4].

The detailed and explicit rules imposed by this Regulation ensured that EU legal requirements were implemented simultaneously in all Member States, filling the existing gaps in national law relating specifically to the use of NMs in consumer products such as cosmetics [6].

Regulation (EC) n.° 1223/2009 entered fully into force on 11 July 2013, and was followed by the publication of Regulation (EC) n.° 655/2013 on the substantiation of cosmetic product claims [7].

In accordance with Article 4 of Regulation (EC) n.° 1223/2009, cosmetic products can be placed on the market only if they have a responsible person (RP) (individual or collective) associated. The RP can be represented by the manufacturer, distributor, or importer of the product, and must ensure compliance with the approved regulation throughout the product's life cycle [8]. Additionally, the RP must guarantee product safety through compliance with good manufacturing practice (GMPs) guidelines, compliance with the Product Information File (PIF), submission of a full notification via CPNP (Cosmetic Product Notification Portal) prior to introduction of the cosmetic product in the market, and communication of undesirable or serious undesirable effects to the competent authorities. Particularly, cosmetics containing NMs must be notified by the RP (see Figure 1) six months before being placed on the market (except for colorants, UV-filters, and preservatives included in the Annexes of the Regulation (EC) n.° 1223/2009) [9].

To demonstrate that a cosmetic product complies with Article 3 of Regulation (EC) n.° 1223/2009, the RP should ensure that the cosmetic product has undergone a rigorous safety assessment and that a cosmetic product safety report (CPSR) is set up in accordance with Annex I of Regulation (EC) n.° 1223/2009 prior to placing a cosmetic product on the market. In this sense, the RP must appoint a safety assessor (SA) who will be responsible for evaluating product safety. This assessor must have a degree in toxicology, pharmacy,

medicine, or a similar course recognized by a MS and a minimum of 3 years prior experience in the field. The CPSR is the most important part of the PIF [10]. This document is mandatory for any product that shall be placed on the market. Its structure, defined by Annex I of Regulation (EC) n.° 1223/2009, comprises two parts: Part A relating to information on cosmetic product safety and Part B relating to cosmetic product safety assessment [8,11].

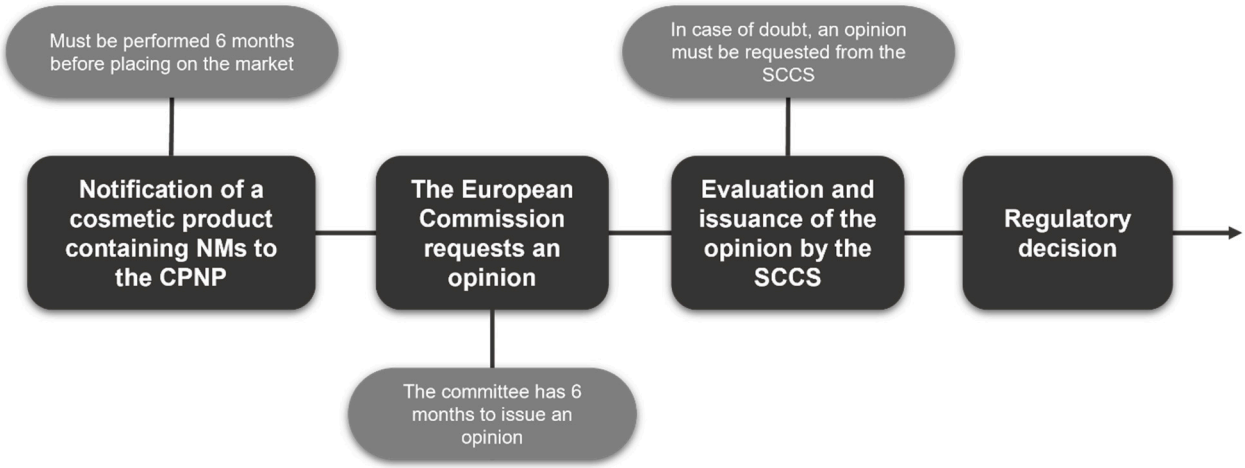

Figure 1. Cascade of processes leading to regulatory decision [5,12]. CPNP—Cosmetic Product Notification Portal; NM—Nanomaterial; SCCS—Scientific Committee on Consumer Safety.

3. Nanomaterials (NMs) in Cosmetics

Article 2, Section k of Regulation (EC) n.° 1223/2009 defines NM as an "insoluble or bio persistent material and intentionally manufactured material, with one or more external dimensions, or an internal structure, on a scale from 1 to 100 nm" [13,14]. Therefore, NMs are so small that they cannot be seen by the human eye. They may be present in nature, or they may be manufactured and added to consumer products to provide very specific properties. Additionally, the physical and chemical properties of particulate materials change when they are manufactured at nanosized dimensions [12,15,16].

Nanotechnology has a wide range of applications and has become an interesting and relevant technology in the biomedical, optical, mechanical, electronic, and cosmetic fields and in the food industry. In the cosmetic field, NMs have been extensively explored as ingredients in cosmetic products [17–20]. However, the changes in the physicochemical properties of a material at nanoscale can lead to changes in their biokinetic and biological interactions and effects, compared with their macrosized equivalents. This means that some NMs could have potential intrinsic hazards that are not observed in their non-nano form and still are not recognized due to a lack of data [7].

There are specific regulatory provisions for cosmetic products containing NMs. However, the provisions of Regulation (EC) n.° 1223/2009 do not apply to NMs used as colorants, UV-filters, or preservatives regulated under Article 14 and listed in Annexes III, IV, V or VI, unless explicitly specified [11].

3.1. Notification of a Cosmetic Product Containing NMs in the CPNP

According to Article 13 of Regulation (EC) n.° 1223/2009, before placing a cosmetic product on the market, the RP must notify to the Commission and submit all the data requested concerning the cosmetic product, via CPNP [21]. Once this information has become available, it can be consulted by regulatory authorities, poison centres, or other MS agencies for the purpose of market surveillance, market analysis, evaluation, and consumer information [22].

The notification of a cosmetic product containing NMs, in addition to the provisions of Article 13 of Regulation (EC) n.° 1223/2009 and according to Article 16, the RP is required

to identify the NM—IUPAC nomenclature, as well as to add some specific denominations—NM specifications, such as physical–chemical properties and particle size, and estimation of the amount of NM contained in cosmetic products to be placed on the market annually—and to provide the correspondent toxicological profile [9,18,23].

Since the NMs listed in Annexes IV, V, and VI of Regulation (EC) n.° 1223/2009 have already been subject to a full risk assessment by the Scientific Committee on Consumer Safety (SCCS), products containing NMs that are present in these annexes (colorants, preservatives, and UV-filters) no longer need to submit a notification under this article. The SCCS is a committee composed of independent experts who provide opinions on the basis of scientific evidence [24]. Their opinions are used to carry out safety assessments and to guide regulatory decisions in the EU and other countries [8]. Furthermore, the committee provides advice from industries to the competent authorities of the MS to ensure strict compliance with Regulation (EC) n.° 1223/2009 [2].

Safety data on NMs is still scarce; therefore, in cosmetic products that contain NMs, a high level of health protection must be ensured. In order to assess the safety of NMs, the SCCS, in collaboration with the competent authorities, should guide test methodologies according to the specific characteristics of the NMs. In this sense and in case of doubt, the EC must immediately request an assessment from the SCCS, which will later issue an opinion on the safe use of NMs [11,24].

Cosmetic products containing NMs that have not undergone a full risk assessment by the SCCS, i.e., all NMs that are not included in Annexes III, IV, V or VI of Regulation (EC) n.° 1223/2009, must submit a notification of a new cosmetic product containing NM [13,25].

After the evaluation of the information and, in case of doubt regarding the safety of a notified NM, the EC must seek the opinion of the SCCS on the safety of the NMs in the relevant categories of the cosmetic products under normal or reasonably foreseeable conditions of use [23,24].

The data required to introduce in the online CPNP portal are the following:

3.1.1. Identification of the Product and the NM

Category of the cosmetic product in which the NM will be incorporated, the class of compound to which the NM belongs, contact details of the RP, and IUPAC name are mandatory requirements. However, other several identifiers of the NM should be entered, namely the International Nomenclature of Cosmetic Ingredients (INCI), the CAS number, the EINECS or ELINCS number, the International Nonproprietary Name (INN), and the XAN number, which is the number approved by a specific country (X) [21,25].

3.1.2. Specifications

Each NM has a unique physical structure and a specific chemical composition. In addition, an NM has several particularities, such as its behavior, smart targeting, and interactions, which are inevitably influenced by the nanodimensions (morphology, size, and surface area) and by the nature of the chemical substances in their constitution. It is true that a NM can be harmful to human health or the environment, mainly because of its chemical composition. However, several other aspects of the NMs can also contribute to their harmful capacity, such as the surface composition, which can affect their absorption, their effects, and toxicokinetics [20]. In this sense, certain physicochemical properties can influence the biological effects, behavior, and properties of an NM. Therefore, it is extremely important that the physicochemical characteristics of an NM in a cosmetic product are disclosed at various stages of the manufacturing process [26].

A complete characterization, as recommended by the SCCS guidance on the safety assessment of NMs in cosmetic products, with particular emphasis on particle size and the physical and chemical properties, must be provided at this stage of the notification. The guidance on the safety assessment of NMs in cosmetics highlights the minimum information requirements that must be provided for the characterization of an NM intended for use in a cosmetic product [21]. A revision of the guidance was published in November

2019 (SCCS/1611/19), whose major change focused on exposure assessment as a safety starting point, in addition to physical–chemical characterization [20].

- Particle size and size distribution, including presence of agglomeration or aggregation: Mean, median, and standard deviation in particle size, size distribution, and weighted sum function must be supplied. Presence of aggregates or agglomerates must be indicated, along with particle number and mass distribution, which is required to be shown graphically, coupled with distribution diagrams [13,27,28].

The European Food Safety Authority (EFSA) and the Organization for Economic Co-operation and Development (OECD) have recommended using more than one method to determine the particle size. In addition, every batch-to-batch difference should also be specified and information on characterization techniques for size assessment should be described. The recommended techniques are Field Flow Fractionation (FFF), disc-Centrifugal Liquid Sedimentation (disc-CLS), Hydrodynamic Chromatography (HDC), Dynamic Light Scattering (DLS), Analytical Ultracentrifugation (AUC), Transmission Electron Microscopy (TEM), Atomic Force Microscopy (AFM), Scanning Electron Microscopy (SEM), High Performance Liquid Chromatography (HPLC), Differential Mobility Analyzer (DMA) and Particle Tracking Analysis/Nanoparticle Tracking Analysis (PTA/NTA) [4,15,16].

- Morphology: In this field, information regarding the physical/crystalline form of the material (amorphous, crystalline, tube, or stick), propensity to aggregation, state of preparation (solution, powder, dispersion, or suspension), and NM aspect ratio (for elongated fiber/tube type materials) must be provided. The data must be properly supported by images obtained by some of the aforementioned techniques [20,27,29].

The characterization methods applied to evaluate the morphology of NMs are principally SEM, TEM, AFM, Field Emission Scanning Electron Microscope (FESEM), Elliptically Polarized Light Scattering (EPLS), Nuclear Magnetic Resonance (NMR), Ferromagnetic Resonance (FMR), 3D-tomography, ray diffraction, and thermal analysis [20,27,28].

- Surface characteristics: Information considering morphology/topography, surface charge (zeta potential), reactive sites, and coatings that may change reactivity characteristics or that are responsible for adding a new function and any biochemical/chemical surface changes must be provided. Information on zeta potential (measured in water or buffer) provides an indication of the strength of surface charge [14,15].
- Solubility: Information regarding the solubility of NM in relevant solvents, such as water and n-octanol, and the partition between the octanol/water partition coefficients must be filled. This information should include dissolution rates, not only for soluble NMs but also for partially insoluble ones, as well as information on the hygroscopicity of the powders [16,30].
- Surface area: Providing information on the specific surface area (SSA) using the Brunauer–Emmett and Teller method (BET method) and volume-specific surface area (VSSA) is mandatory for dry powders only [21]. The BET method measures the particle SSA by dividing the absolute surface area by the sample mass analyzed giving the so-called mass-specific surface area, reported in m^2/g. The VSSA is calculated from the SSA using the density of the NM in question and is expressed in m^2/cm^3 [15,31].
- Catalytic activity: Indication concerning the chemical reactivity of the surface of the NM and information on the possible potential of photocatalytic activity must be disclosed. It should also be indicated if the core material is doped, meaning if the NM contains intentionally introduced materials for the purpose of modulating certain chemical, biochemical, or catalytic reactivity [27,32].

3.1.3. Quantity

In this field, information on the estimate of the amount of NM present in the product to be placed on the market on an annual basis must be provided. The estimate should be expressed in kg [20,26].

3.1.4. Toxicological Profile of the NM

In this field of information, the toxicological profile of the NM must be supplied [21]. This information has to fulfill the requirements established by SCCS in the "Guidance on the Safety Assessment of Nanomaterials in Cosmetics" [26], and the outline of the toxicological studies must be reported, including data such as percutaneous absorption, toxicokinetic, acute toxicity, irritation and corrosivity, skin sensitization, mutagenicity/genotoxicity, repeated dose toxicity, carcinogenicity, reproductive toxicity, and photo-induced toxicity according to the correspondent species, mainly human data, if available [25]. This is because, prior to the release of Regulation (EC) n.° 1223/2009, toxicological data were obtained through experimental research on animals using the same exposure routes as humans. These studies were banned since 11 July 2013, and alternative validated methods have been developed for safety determination and safety assessment, although they are not validated for NMs. Since validated alternative methods that can be used in place of animal tests are not yet available for NMs, the SCCS can accept results from methods that may not have been formally validated for NMs but have been demonstrated to be scientifically valid for danger identification of NMs [24,26].

3.1.5. Safety Data

The safety data of the NM must be provided as a safety data file by the RP (or their delegate), who must possess a risk assessment based on hazards identified in the toxicological profile and the exposure conditions of the NM regarding the category of the cosmetic product. The provided safety data file should be in line with all the criteria recommended by the SCCS in the "Guidance on the Safety Assessment of Nanomaterials in Cosmetics" (SCCS/1484/12) and "Testing of Cosmetic Ingredients and their Safety Evaluation" (SCCS/1416/12) [21].

The SCCS guidance accepts that derivation of toxicological point of departure for the calculation of the MoS of a new cosmetic ingredient may not be possible, or only possible in exceptional cases, along with the estimate of internal exposure, without the possibility of animal testing. Data obtained to comply with other non-cosmetic regulations, such as under the REACH Regulation, should be used and submitted when available [23].

The REACH is Regulation (EC) 10907/2006 that governs the registration, evaluation, authorization, and restriction of chemicals in the EU. This regulation, came into force on 1 June 2007, and aims to protect health and the environment against the risks that chemicals can induce; it also contributes to the promotion of the development of alternative methods of evaluating the safety of substances, while at the same time contributing to reinforcing innovation and competitiveness in EU companies [8]. REACH regulation provisions are based on the precautionary principle, which assigns manufacturers, importers, and users the responsibility to ensure that the substances they manufacture, market, and use do not adversely affect human health and the environment [33]. Both raw chemical materials and finished products are impacted by REACH regulation, and among them are cosmetic products, which are considered chemical preparations under this regulation [34].

Moreover, additional information that is relevant for the safety assessment of the NM should be stated [21].

3.1.6. Exposure Conditions

Information regarding exposure conditions, as well as the amount of substance and the frequency of human exposure to the cosmetic product must be provided [11,13]. There are currently no indicators that show that the use of conventional cosmetic products is different from the use of other products containing NM. In this sense, the SCCS considers that the assessment of exposure conditions for conventional cosmetic ingredients also applies to cosmetics with NM. However, it is emphasized in the guidance that special considerations of the nano-aspects will need to be considered [26], namely type of cosmetic product (whether the cosmetic product is a rinse-off or a leave-on product, which impacts the exposure time on the skin); the exposure route (oral, nasal, or topical); and the concentration

of the NM in the product (% *w*/*w*). Likewise, information considering expected exposure conditions must also be specified (see Table 1).

Table 1. Expected exposure conditions information [4,35].

(1) Range of cosmetic products indicated for the use of NM	(7) Improper applications that may increase exposure
(2) Percentage of ingredient, by weight, of the final cosmetic product	(8) Absorbed fraction or amount likely to enter the body
(3) Amount of product to be applied in each use	(9) Application on dermal areas exposed to sunlight
(4) Application frequency	(10) On the basis of the intended use of the product, dermal exposure, oral exposure, or inhalation exposure must be estimated
(5) Skin contact area and duration of exposure	(11) Specific area of exposure
(6) Different target groups, such as people with compromised or damaged skin or children, where relevant	(12) Any other relevant information

NM—Nanomaterial.

4. Labeling Information

Cosmetic products can be placed on the market only if they comply with the labeling rules stated in Article 19 of Regulation (EC) n.° 1223/2009, which mentions that container and packaging must contain mandatory information in indelible, easily legible, and visible lettering.

Regarding NMs, if the cosmetic product contains them as ingredients, they must be clearly highlighted. The names of the NM ingredients must be followed by the word 'nano' in brackets [5,16,25].

5. NMs in EU Market

As stated in article 16 of Regulation (EC) n.° 1223/2009, the EC must publish a catalogue with all NMs in use in cosmetic products placed on the European market [5]. This catalogue, available to all consumers, is regularly updated. The latest version, released in 2019, listed 29 NMs currently in use in cosmetics [2]. The catalogue lists the names of the NMs, submitted to the CPNP, according to the INCI designation.

However, being registered in the catalogue does not mean being authorized [13]. The catalogue is based solely on information provided by the RP to CPNP, so, the accuracy of the information has not been verified. Thus, the catalogue only provides information on the NMs used in cosmetic products and does not constitute a list of authorized NMs [35]. Most of these substances are also registered under the REACH regulation [2,33].

The catalogue is divided in NMs used as colorants, preservatives, UV filters, and used with other functions [9,11]. In addition, the catalog indicates the exposure conditions and the categories of cosmetic products in which these NMs can be found [2,4]. Currently, only five NMs are authorized by the EC for use in cosmetic products, namely carbon black (nano) (for use as a colorant), titanium dioxide (nano), zinc oxide (nano), methylene bis-benzotriazolyl tetramethylbutylphenol (MBBT) (nano), and tris-biphenyl triazine (TBPT) (nano) (for use as UV filters). In order to obtain authorization for using a NM as a UV filter, colorant, or preservative in a cosmetic product, authorization must be sought from the EC, which will subsequently ask the SCCS for an opinion on the NM [10].

After receiving a request from the Commission, the SCCS has six months to provide an opinion [35]. If the SCCS determines that it is essential, the Commission asks the RP to supply any missing data within a reasonable and specifically stated timeframe that cannot be extended. The SCCS must establish whether the use of a NM is safe and, if necessary, include limitations or restrictions. However, due to the lack of data or information submitted to the SCCS or available in scientific literature, this is not always possible [18,25].

According to data extracted from the CPNP and published in the latest Report from the commission on the use of NMs in cosmetics and on the review of Regulation (EC) n.° 1223/2009 on cosmetic products regarding NMs, between 2013 and 2020, 37,647 cosmetic products were reported with NMs in accordance with Article 13. This number corresponds to approximately 1.5% of all notifications of cosmetics. There were 1445 notifications made under Article 16. This results in an annual average of 3620 new products containing NMs that are reported to the CPNP, i.e., approximately 10 products containing NMs enter the EU market daily [36].

In 2020, 3444 notifications were communicated under Article 13 of NMs listed in Annexes IV, V, and VI, while only 137 notifications were filed under Article 16. The majority of cosmetic products containing NMs are ingredients with a coloring or UV-filter function [23,27,36].

The NMs listed in annexes IV, V, and VI, used as colorants, preservatives, or sunscreens, respectively, are not subject to notification requirements under Article 16, as they are already subject to a prior EC authorization regime to be placed on the market. Since NMs were already approved by EC as other cosmetic ingredients, they can be submitted under Article 13 of Regulation (EC) n.° 1223/2009. The NMs present in the aforementioned annexes are Carbon Black (nano) as colorant and Methylene Bis-Benzotriazolyl Tetramethylbutylphenol (nano), Titanium Dioxide (nano), Tris-Biphenyl Triazine (nano), and Zinc Oxide (nano) as UV filters [13,20].

Portraying more than 70% of notifications of cosmetic products containing NMs to CPNP, the Report from the commission on the use of NMs in cosmetics and on the review of Regulation (EC) n.° 1223/2009 on cosmetic products regarding NMs states that the four main NMs used are (i) titanium dioxide, (ii) silica dimethyl silylate, silane, dichlorodimethyl, silica reaction products, (iii) nano carbon black (CI 77266), and (iv) silica. Sun protection, nail varnish/nail makeup, oxidative hair care, foundation, lip care products, and lipstick are the most common product categories associated with these NMs [36].

5.1. Titanium Dioxide (TiO_2)

Titanium dioxide (TiO_2) is a highly valuable excipient in pharmaceutical industry owing to its application as an opacifier and colorant. Furthermore, it provides protection of active substances from UV light and is used in several products, namely orthodontic composites, paints, food additives, and cosmetics. As a cosmetic ingredient, its microcrystalline form (200–400 nm) is used as a white pigment, acting as an opacifier in products such as toothpastes, paints, or sunscreens. When used as a UV filter, the microform leaves a white residue on the skin and clothes, and consumer acceptability is low. In the nanoform (1–100 nm), it is used only as a UV filter, and it is able to reflect and refract both ultraviolet A and B radiations, contributing to the prevention of sunburns and skin cancer [37,38]. Moreover, nanosize particles are able to reduce the reflection of visible light, making the NPs appear transparent on the skin resulting in enhanced aesthetics. The nanosize also improves their spreadability, according to its application in sunscreens [2,39,40].

Therefore, its nanoform can be applied primarily in sunscreens as well as in leave-on products, such as foundations, daily creams, or lip balms [37,40]. According to "Revision of the opinion on Titanium Dioxide, nano form" published by SCCS [41], the use of TiO_2 is considered to "not pose any risk of adverse effects in humans after application on healthy, intact or sunburnt skin" in a concentration up to 25% in sunscreens. However, this is not valid for applications where there is a risk of inhalation, such as sprays [42]. The SCCS "Opinion on Titanium Dioxide (nano form) as UV-Filter in sprays" does not recommend the use of TiO_2 (nano) as an ingredient in spray products due to the possibility of accumulation in the lungs after inhalation [41]. Under Regulation (EC) n.° 1223/2009, this nano ingredient is prohibited in products that possess the risk of product inhalation [5,42].

To be used as an ingredient, TiO_2 (nano) should comply with specific physical chemical characteristics: (i) must possess high purity $\geq$99%; (ii) be present in the rutile form, or rutile with anatase up to 5%, with crystalline structure and with a physical appearance as

clusters of spherical, needle, or lanceolate shapes; (iii) its median particle size based on number size distribution should be ≥30 nm; (iv) can be coated with silica, hydrated silica, alumina, aluminum hydroxide, aluminum stearate, stearic acid, trimethoxycaprylysilane, glycerin, dimethicone, hydrogen-dimethicone, simethicone, a combination of silica at a maximum concentration of 16% and cetyl phosphate at a maximum concentration of 6%, a combination of alumina at a maximum concentration of 7% and manganese dioxide at a maximum concentration of 0.7%, a combination of alumina at a maximum concentration of 3% and triethoxycaprylylsilane at a maximum concentration of 9%; (v) should possess photocatalytic activity ≤10%; and (vi) the particles should be stable in the final formulation [5,39].

5.2. Methylene Bis-Benzotriazolyl Tetramethylbutylphenol (MBBT)

This NM, also known as Tinosorb® M, is approved as a UV filter in sunscreens, skin lightening products, and other daily care products. In terms of systemic effects, SCCS states that there is no concern for the dermal application of the product, as it can be used in concentrations up to 10%. However, with regard to application in products that can lead to pulmonary exposure, and since information on inhalation toxicity is limited, caution should be exercised with this type of exposure [43]. Although, a study linked MBBT to contact dermatitis and allergic dermatitis in adults, the data were found to be inconclusive due to the presence of decyl glucoside, the surfactant used in MBBT-containing products [44,45].

According to Regulation (EC) n.° 1223/2009, this NM cannot be used in products that could lead to pulmonary exposure by inhalation. In addition, it is also regulated that NMs can only be used under the following conditions: (i) degree of purity ≥98.5%, and the isomer fraction of 2,2′-methylene-bis-(6(2H-benzotriazolo-2-yl)-4-(iso-octyl-)phenol) must not be greater than 1.5%; (ii) should exhibit solubility <5 ng/L in water at a temperature of 25 °C; (iii) partition coefficient (Log Pow) of 12.7 at 25 °C; (iv) should be used uncoated; and (v) must possess median particle size D50 value (50% of the number below this diameter) ≥120 nm of mass distribution and/or ≥60 nm of numerical distribution by particle size [5,46].

5.3. Tris-Biphenyl Triazine (TBPT)

This NM, also known as Tinosorb® A2B (TBPT), was the first UV filter to be added to Annex VI of Regulation (EC) n.° 1223/2009 [47]. This organic NM along with MBBT can provide protection against UVA1, UVA2, and UVB radiation, making them highly effective UV filters [48]. In the SCCS's opinion the concentration of the uncoated form, with a median particle size >80 nm, can reach up to 10% of a cosmetic product [49]. Like other NMs, it cannot be used in sprays (aerosols) due to the risk of pulmonary exposure, should possess a degree of purity ≥98%, and should be used uncoated and with a median primary particle size >80 nm [5].

5.4. Nano Carbon Black (CI 77266)

This coloring ingredient has been used in various make-up products [50], such as eye pencils, mascaras, shadows, eyeliners, eyebrow products, nail enamels, and foundations, for a long time [13]. The SCCS opinion considers that, depending on the product, the concentration of this ingredient can vary between 0.001% and 10%, and in skin care products, its concentration is 0.001%; in enamels and mascaras, it can present a concentration of up to 5%, and in decorative products intended to be used in the eyes, it may have a concentration of up to 10%. For NPs larger than 20 nm, the SCCS considers that there is often no skin absorption and no risk of negative consequences after application to healthy, intact skin [51]. Thus, Regulation (EC) n.° 1223/2009 stipulated that the maximum concentration of this NM in a ready-to-use product is 10%, and it cannot be used in products that may lead to pulmonary exposure by inhalation. In addition, the regulation also defined that in order for the NM to be incorporated in cosmetics, it should present the following characteristics: (i) a degree of purity >97%, with ash content ≤0.15 %, total sulfur

≤0.65%, total PAH ≤500 ppb, benzo(a)pyrene ≤5 ppb, dibenzo(a, h)anthracene ≤5 ppb, total As ≤3 ppm, total Pb ≤10 ppm, and total Hg ≤ 1 ppm as impurities, if present; and (ii) a primary particle size ≥20 nm [51].

5.5. Silica Dimethyl Silylate, Silane, Dichlorodimethyl, Silica Reaction Products, and Silica Nanoparticles

These NPs varies between 5 and 100 nm in size and are capable of encapsulating hydrophilic and lipophilic substances. They can be found in several rinse-off products for use on the face, hair, skin, and nails, and above all, in leave-on products. These NMs have emollient, emulsifier, and aqueous barrier functions, increased spreadability, effectiveness, and texture, which reduce degradation and increase shelf life of the products. They are also used in lipsticks in order to improve their appearance and pigment distribution, preventing the lipstick from migrating out of the lip. They can also be found in deodorants, make-up products, hair styling, toothpastes, and sunscreens. The cosmetic industry's interest in this type of NMs has increased since, in addition to having a hydrophilic surface, they also have a low production cost [2,17].

Questions were raised by the committee concerning the potential for these NPs to break away from their clusters and enter cells, potentially causing toxicity [52,53]. In this regard, SCCS emitted an opinion on the safety of the various types of silica nanoparticles. After a detailed evaluation, the final verdict of the opinion proved to be inconclusive, since the evidence, both provided in the submission and available in the literature, proved to be insufficient and inadequate to draw any conclusion in favor of or against the safety of these NMs [54].

6. Sustainability in Cosmetic Industry

In recent years, there has been a growing concern about the environmental and social impact that the cosmetic industry has on the environment. Not only consumers but also manufacturers, organizations, and researchers have become interested in sustainability towards cosmetic products [55,56].

Sustainability can present different interpretations; however, the idea of sustainability emerged from the concept of sustainable development, i.e., a development that is able to meet current needs without compromising future generations and their needs. Even though sustainability effects should be considered throughout a product's life cycle, the choice of raw materials in cosmetic industry requires more focus because the available information is still fragmented and scattered. Therefore, replacing synthetic substances with more sustainable ones is one of the major challenges [57,58].

Regarding NMs, there are several measures that must be adopted by researchers to develop innovative and sustainable cosmetic products, including the application of natural NMs obtained from renewable by-products, the choice of methods with minimal operational steps, and the employment of formulation methods that avoid or minimize the use of toxic solvents, among others [19].

7. Regulatory Harmonization

Although comparable, the six major markets' definitions of "cosmetic product" present minor differences (EU, USA, Canada, Japan, China, and Brazil). These definitions are typically based on the product's functions, the body parts to which it is administered, the application method, the indication of use, the claims, and the opinions of the consumers. However, in practice, cosmetics products vary by region [10].

Concerning NMs, the EU was the first jurisdiction to create explicit restrictions for the use of NMs in cosmetics. Although, the fact that these have numerous advantages has made them a global phenomenon, leading to the adoption of specific regulations by other regions [13]. Thus, efforts are currently being undertaken to harmonize the definition of NM and to align policies considering the safety assessment of NMs in various international bodies. The International Cooperation on Cosmetics Regulation has worked towards

harmonizing experimental procedures to reach a consensus on safety approaches for NMs in cosmetics [9,25,35].

8. Concluding Remarks

In July 2021, the EC published the latest report on the use of NMs in cosmetics and on the review of the provisions of the Regulation (EC) n.° 1223/2009 on cosmetic products regarding NMs. The report states that "the use of NMs in cosmetic products is limited (1.5% of all products) and seems to be rather stable over the past five years (2016–2020)"; nevertheless, they concluded that, on average, approximately 10 products containing NMs enter the EU market daily [36].

Regulatory decisions are made by the commission on the basis of the opinions of the SCCS, which in the last 10 years, has published 20 opinions. The assessment performed by the SCCS, which later gives rise to the opinion, is based on information provided by the notifier to CPNP, both in the original notification and in additional notifications, where applicable. However, due to insufficient data/information submitted by the applicants and/or available in the scientific literature, SCCS may not be able to find a way to formulate safety conclusions.

Unfortunately, seven out of ten opinions did not reach plausible conclusions regarding the safety of the NM undermining the commission's ability to move forward with regulatory decisions. Since the SCCS has only 6 months to formulate an opinion, at the end of this period, the RP can place the product on the market, regardless of the opinion's outcome.

It would be important to improve the notification process via CPNP, namely regarding the 6-month period defined by Regulation (EC) n.° 1223/2009, and to study the possibility of extending the current authorization system described in Article 14 regarding colorants, preservatives, and sunscreens that include NMs.

On the other hand, in 2020, interesting findings were published from a study titled "Understanding the Public's Perception of Nanomaterials and How Their Safety Is Perceived in the EU", issued by the European Union Observatory for NMs (EUON) and the European Chemicals Agency (ECHA). This report found that nearly nine out of ten respondents (EU citizens) felt it was important to be informed when purchasing a product containing NMs. The study also showed that if respondents had received clear information concerning the NMs contained in the product, most would adopt a prudent stance, not buying the product, or making a decision based on its category. The negative attitude towards NMs was associated with their level of knowledge about them.

This lack of knowledge could be overcome through communication with users using digital technologies, for example, an electronic label with information on the use of cosmetic ingredients, namely NMs.

NMs are continually emerging in consumer products worldwide. To guarantee sustainability in the use of NMs in cosmetic products, it is essential to conduct detailed risk assessments that minimize their potential negative impacts on human health and the environment. Therefore, the various international bodies responsible for the harmonization of cosmetic regulatory policies must implement guidelines and normalize their toxic evaluation, focusing on the improvement of conventional toxicity testing methods or the development of new approaches, with the aim of determining a complete set of information and available data that can prove the safety of the cosmetic product in the intended conditions of use.

In summary, the application of NMs in cosmetic products not only have noteworthy advantages but also several concerns, in addition to the responsibility to ensure that its application aligns with the practice of sustainability in the industry.

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Abbreviations

AFM: Atomic Force Microscopy; AUC: Analytical Ultracentrifugation; BET: Brunauer–Emmett and Teller method; CPNP: Cosmetic Products Notification Portal; DLS: Dynamic Light Scattering; disc-CLS: disc-Centrifugal Liquid Sedimentation; EC: European Commission; ECHA: European Chemicals Agency; EPLS: Elliptically Polarized Light Scattering; EU: European Union; EUON: European Union Observatory for Nanomaterials; FESEM: Field Emission Scanning Electron Microscope; FFF: Field Flow Fractionation; FMR: Ferromagnetic Resonance; HDC: Hydrodynamic Chromatography; HPLC: High Performance Liquid Chromatography; MBBT: Methylene bis benzotriazolyl tetramethylbutylphenol; MS: Member State; NM: Nanomaterial(s); NMR: Nuclear Magnetic Resonance; NP: Nanoparticle(s); PIF: Product Information File; REACH regulation: Regulation (EC) 10907/2006 concerning the Registration, Evaluation, Authorization and Restriction of Chemical; RP: Responsible Person; SA: Safety Assessor; SCCS: Scientific Committee on Consumer Safety; SEM: Scanning Electron Microscopy; SSA: Specific Surface Area; TBPT: Tris-biphenyl triazine; TEM: Transmission Electron Microscopy; VSSA: Volume—Specific Surface Area; XRD: X-ray Diffraction.

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