Nanomaterials in Cosmetics

Subjects: Nanoscience & Nanotechnology

Contributor: Laura Ferreira , Patrícia C. Pires , Mariana Fonseca , Gustavo Costa , Prabhanjan Shridhar Giram , Priscila Gava Mazzola , Victoria Bell , Filipa Mascarenhas-Melo , Francisco Veiga , Ana Cláudia Paiva-Santos

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. 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. 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.

nanomaterial nanotechnology regulation

1. Identification of the Product and the NM

Category of the cosmetic product in which the nanomaterials (NMs) will be incorporated, the class of compound to which the NM belongs, contact details of the responsible person (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) [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 [2]. 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 .

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 [3]. 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 [2].

- 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 [4][5][6].

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) [7][8][9].

- 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 [2][5][10].

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 [2][5][6].

- 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 [11][8].

- 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 [9][12].

- 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 [3]. 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 [8][13].

- 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 [5][14].

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 [2][15].

4. Toxicological Profile of the NM

In this field of information, the toxicological profile of the NM must be supplied [3]. This information has to fulfill the requirements established by SCCS in the “Guidance on the Safety Assessment of Nanomaterials in Cosmetics” [15], 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 [1]. 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 [16][15].

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) [3].

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 [17].

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 [18]. 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 [19]. 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 [20].

Moreover, additional information that is relevant for the safety assessment of the NM should be stated [3].

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 [21][4]. 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 [15], 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 [7][22].

(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.

References

1. Santana Cabello, R.; Gañán Rojo, P.; Zuluaga, R Lessons from the European Regulation 1223 of 2009, on Cosmetics: Expectations Versus Reality . *NanoEthics* **2019**, *13*, 21–35, https://doi.org/10.1007/s11569-019-00335-6.
2. Gupta, V.; Mohapatra, S.; Mishra, H.; Farooq, U.; Kumar, K.; Ansari, M.J.; Aldawsari, M.F.; Alalaiwe, A.S.; Mirza, M.A.; Iqbal, Z; et al. Nanotechnology in Cosmetics and Cosmeceuticals—A Review of Latest Advancements. *Gels* **2022**, *8*, 173, https://doi.org/10.3390/gels8030173.
3. Directorate-General for Internal Market, Industry, Entrepreneurship and SMEs. Guide to Using CPNP (Cosmetic Products Notification Portal); European Commission: Brussels, Belgium, 2017; Available online: https://ec.europa.eu/docsroom/documents/29563/attachments/1/translations/en/renditions/native (accessed on 24 November 2022)
4. Pastrana, H.; Avila, A.; Tsai, C.S.J Nanomaterials in Cosmetic Products: The Challenges with regard to Current Legal Frameworks and Consumer Exposure. *NanoEthics* **2018**, *12*, 123–137, https://doi.org/10.1007/s11569-018-0317-x.
5. Meinke, M.C.; Lademann, J.; Knorr, F.; Patzelt, A.; Lohan, S.B. 7. Nanocosmetics. In Nanoscience and Nanotechnology; Van de Marcel, V., Eds.; De Gruyter: Berlin, Germany, 2018; pp. 101–116.
6. Pan, G.-H.; Barras, A.; Boussekey, L.; Qu, X.; Addad, A.; Boukherroub, R Pan, G.-H.; Barras, A.; Boussekey, L.; Qu, X.; Addad, A.; Boukherroub, R. *Langmuir* **2013**, *29*, 12688–12696, https://doi.org/10.1021/la4029468.
7. Karamanidou, T.; Bourganis, V.; Gatzogianni, G.; Tsouknidas, A A Review of the EU's Regulatory Framework for the Production of Nano-Enhanced Cosmetics. *Metals* **2021**, *11*, 455, https://doi.org/10.3390/met11030455.
8. Lin, P.-C.; Lin, S.; Wang, P.C.; Sridhar, R Techniques for physicochemical characterization of nanomaterials. *Biotechnology Advances* **2014**, *32*, 711–726, https://doi.org/10.1016/j.biotechadv.2013.11.006.
9. Hartmann, S.F.; Eckert, R.W.; Knoth, D.; Keck, C.M. Characterization of Nanoparticles for Cosmetic Applications. In Nanocosmetics: From Ideas to Products; Cornier, J., Keck, C.M., Van

de Voorde, M., Eds.; Springer International Publishing: Cham, Switzerland, 2019; pp. 181–198.

10. Popović, Z.V.; Dohčević-Mitrović, Z.; Šćepanović, M.; Grujić-Brojčin, M.; Aškrabić, S Raman scattering on nanomaterials and nanostructures. *Annalen der Physik* **2011**, *523*, 62–74, https://doi.org/10.1002/andp.201000094.
11. Bhattacharjee, S DLS and zeta potential – What they are and what they are not?. *Journal of Controlled Release* **2016**, *235*, 337–351, https://doi.org/10.1016/j.jconrel.2016.06.017.
12. ISO. ISO/TR 13014, 2012 Nanotechnologies—Guidance on Physico-Chemical Characterization of Engineered Nanoscale Materials for Toxicologic Assessment. 2012. Available online: https://www.iso.org/standard/52334.html (accessed on 27 November 2022).
13. Baer, D.R Application of surface analysis methods to nanomaterials: Summary of ISO/TC 201 technical report: ISO 14187, 2011—Surface chemical analysis—Characterization of nanomaterials. *Surf. Interface Anal.* **2012**, *44*, 1305-1308, https://doi.org/10.1002/sia.4938.
14. Petersen, R. Nanocrystals for Use in Topical Cosmetic Formulations and Method of Production Thereof. U.S. Patent WO2008058755A1, 25 February 2010.
15. European Commission, Directorate-General for Health and Food Safety. Guidance on the Safety Assessment of Nanomaterials in Cosmetics: Publications Office; European Commission: Luxembourg, 2020.
16. Vinardell, M.P The use of non-animal alternatives in the safety evaluations of cosmetics ingredients by the Scientific Committee on Consumer Safety (SCCS). *Regul. Toxicol. Pharmacol* **2015**, *71*, 198–204, https://doi.org/10.1016/j.yrtph.2014.12.018.
17. Dhawan, S.; Sharma, P.; Nanda, S. Chapter 8—Cosmetic nanoformulations and their intended use. In Nanocosmetics; Elsevier: Amsterdam, The Netherlands, 2020; pp. 141–169.
18. Ferreira, M.S.; de Oliveira, A.P.; Oliveira, R.; de Oliveira, R.P.; Lobo, J.M.S.; Almeida, I. Regulamentação dos produtos cosméticos: Uma perspetiva da evolução em Portugal e na União Europeia. Acta Farm. Port. 2021, 10, 15. Available online: https://actafarmaceuticaportuguesa.com/index.php/afp/article/view/243 (accessed on 14 December 2022).
19. Regulation (EC) n.° 1907/2006 of 18 December 2006 Concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). 2006. Available online: http://data.europa.eu/eli/reg/2006/1907/2014-04-10 (accessed on 5 December 2022).
20. ECHA. Understanding. Available online: https://echa.europa.eu/regulations/reach/understanding-reach (accessed on 13 December 2022).
21. Pauwels, M.; Rogiers, V EU legislations affecting safety data availability of cosmetic ingredients. *Regulatory Toxicology and Pharmacology* **2007**, *49*, 308–315, https://doi.org/10.1016/j.yrtph.200

7.08.009.

22. Scientific Committee on Consumer Safety The SCCS guidance on the safety assessment of nanomaterials in cosmetics. *Regulatory Toxicology and Pharmacology* **2020**, *112, 104611*, 112, 104611, https://doi.org/10.1016/j.yrtph.2020.104611.