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SweNanoSafe

Swedish National Platform for Nanosafety

Review of regulation relevant to nanomaterials in the EU and Sweden

Preface

SweNanoSafe is a national platform for the safe handling of nanomaterials; its purpose is to contribute to achieving the environmental quality objective of a non-toxic environment and protect human health. SweNanoSafe is an assignment from Miljödepartementet – the Ministry of the Environment through the Swedish Chemicals Agency (KEMI).

The objective of the platform is to spread knowledge and provide special support to the authorities in matters relating to the safe handling and use of nanomaterials. SweNanoSafe brings together academia, authorities, industry and organisations for a common dialogue regarding nanosafety. This also includes identifying needs for the safe handling of nanomaterials and contributing with proposals for solutions and concrete measures that meet these needs, as well as working actively for improved nanosafety. Since 2019, SweNanoSafe's operations have been conducted at the Institute for Environmental Medicine, Karolinska Institutet, and include an Expert Panel, a Council of Authorities, Research Network, an Education Network, as well as a group for Operations Coordination which coordinates activities such as workshops and communication via the platform's website.

This report provides an overview of the legislation relevant to nanomaterials within the EU and in Sweden. The report has been compiled to support national authorities in their role as responsible bodies for oversight and regulatory guidance, as well as to provide an overview of the different areas of legislation that may be relevant to different types of operators from industries affected by the use or handling of nanomaterials. The objective of the report has not been to provide a comprehensive picture of the area, but to briefly and concisely point to various sources of additional information for those who need to further investigate specific areas of legislation.

The report has been compiled by Gen Shao and Penny Nymark (SweNanoSafe) and has been reviewed by SweNanoSafe's council of authorities consisting of Gregory Moore (KEMI), Elmira Tavoosi (Läkemedelsverket – Medical Products Agency), Julia Taylor (Naturvårdsverket – Swedish Environmental Protection Agency), Christer Idström (Boverket – Swedish National Board of Housing, Building and Planning), Gustav Bäck (Arbetsmiljöverket – Swedish Work Environment Authority), Linda Molander (Folkhälsomyndigheten – Swedish Public Health Agency, Daniel Edgar (Livsmedelsverket – Swedish National Food Agency), and by Anna Bergström and Bengt Fadeel, SweNanoSafe's steering group.

SweNanoSafe, 19 May 2023

SweNanoSafe

National Platform for Nanosafety

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Content

INTRODUCTION

The safety of nanomaterials is regulated within several EU legislative frameworks. To support the national government agencies within their sectorial responsibilities, and also provide an overview to industries that manufacture, import, use or distribute products containing nanomaterials regarding regulatory domains that may be of relevance for their activities, a summary and detailed explanation of EU and national regulations that explicitly address nanomaterials is provided here.

Table 1 summarises the EU chemical regulation REACH and other product-specific regulations (e.g., cosmetics, biocidal product, medical devices, and food-related products) explicitly addressing nanomaterials. The second section provides further detail on these legislative provisions and the regulation for Classification Packaging and Labelling. In particular, reference to the roles and responsibilities of national authorities and EU authorities and committees (e.g., ECHA, EFSA, SCCS) is detailed.

In 2011, the EU Commission adopted the Recommendation 2011/696/EU, aiming to support a consistent definition for nanomaterials within different sectorial legislation with specific provisions for nanomaterials. In addition, the EC-Joint Research Centre has provided an overview of concepts and terms used in the European Commission's definition of nanomaterial in order to support the implementation of such a definition. On 10th June 2022, the Commission revised the recommended definition of nanomaterials. It is expected that different legislative frameworks will update their legal binding definitions of nanomaterials based on this revision, in accordance with their own timetables.

TABLE 1. OVERVIEW OF EU REGULATIONS EXPLICITLY ADDRESSING NANOMATERIALS

Regulation	Definition	Approval procedure specifically for NMs	Labelling for nanomaterial content	Scope	Agency or Scientific committee assisting the implementation	Guidance[#]
REACH (Regulation 1907/2003) and amendment (Regulation 2018/1882)	Nanoform	No	/	Human safety Environment	European Chemicals Agency	Nanomaterials - ECHA (europa.eu)
Biocidal Products Regulation (EU) No. 528/2012	Nanomaterial	Yes	The label must show the name of each NM followed by the word “nano” in brackets.	Human safety Environment	European Chemicals Agency	/
Cosmetics Regulation (EC) No. 1223/2009	Nanomaterial	Yes	The names of NM-ingredients shall be followed by the word ‘nano’ in brackets	Human safety	Scientific Committee on Consumer Safety	Guidance on the safety assessment of nanomaterials in cosmetics - Publications Office of the EU (europa.eu)
Novel Food Regulation (EC) No. 2015/2283	Engineered nanomaterial	Yes	Under FIC Regulation 1169/2011	Human safety	European Food Safety Authority	Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: human and animal health | EFSA (europa.eu)
Food additives Regulation (EC) No.	/	No	Under FIC Regulation	Human safety	European Food Safety Authority	Guidance on risk assessment of

1333/2008			1169/2011			nanomaterials to be applied in the food and feed chain: human and animal health | EFSA (europa.eu)
Plastic Food Contact Materials Regulation (EC) No. 10/2011	/	Yes	/	Human safety	European Food Safety Authority	/
Active and Intelligent FCM Regulation (EC) No 450/2009	/	Yes	/	Human safety	European Food Safety Authority	/
Provision of Food information to Customers Regulation 1169/2011	Nanomaterial	/	/	/	/	/
Medical devices Regulation (EC) No. 2017/745	Nanomaterials	Yes	Special attention shall be given to nanomaterials	Conformity assessment	Joint Research Centre; European Medicines Agency; Notified Bodies assigned by Member States	ISO - ISO/TR 10993-22:2017 - Biological evaluation of medical devices — Part 22: Guidance on nanomaterials

#: the detailed guidance can be found below

EXAMPLES OF EXISTING LEGISLATIVE PROVISIONS AND THE ROLE OF EFSA, ECHA, SCCS

REACH REGULATION

In general, REACH Regulation (Registration, Evaluation, Authorisation and Restriction of chemicals (EC) No. 1907/2006) places the responsibilities for chemical safety at the industry. To comply with the regulation, companies need to register their substances they manufacture and market in the EU. Information on the properties and hazards of substances must be documented. Companies have to demonstrate to ECHA how the substance can be safely used, and they must communicate the risk management measures to the users. ECHA receives and evaluates individual registrations for their compliance and the EU Member States evaluate selected substances to clarify initial concerns for human health or for the environment. Authorities and ECHA's scientific committees assess whether the risks of substances can be managed. If the risks cannot be managed, authorities can restrict the use of substances in different ways. Member State Competent Authorities are also responsible for the enforcement of REACH regulations.

Commission Regulation (EU) 2018/1881, as an amendment to the REACH Regulations, provides the definition of ¨nanoforms¨ based on the Commission Recommendation on the definition of a nanomaterial 2011/696/EU, and explicit legal requirements applied for companies (registrants) that manufacture or import nanoforms. If the use of total volume of a substance that covers nanoforms exceeds 1 tonne or more per year per industry (including all nanoforms and non-nanoforms), registrants are obliged to submit NM-specific information to ECHA, including i) characterisation of nanoforms or sets of nanoforms covered by the registration (Annex VI); ii) chemical safety assessment (Annex I); iii) registration information requirements (Annexes III and VII-XI), involving human and environmental toxicological endpoints; and iv) downstream user obligations (Annex XII). Besides, Regulation (EC) No. 2020/878, as an amendment to Annex II of the REACH Regulations, describes the requirements for the preparation of safety data sheets addressing nanoforms.

ECHA provides and updates guidance which explicitly address nanoforms, to registrants (i.e., manufactures and importers) and downstream users, including i) How to prepare registration dossiers covering nanoforms; ii) Guidance on Information Requirements and Chemical Safety Assessment for Nanomaterials; and iii) Appendix for nanoforms applicable to the Guidance on Registration and Substance Identification. In addition, ECHA supports the implementation of REACH by cooperation with other stakeholders. For example, ECHA hosts webinars to inform and discuss the latest developments regarding REACH processes related to nanomaterials, and to help registrants prepare and submit dossiers that involve nanomaterials. ECHA also share the experience

with, and generates consensus among, MSCAs concerning safety information for nanomaterials in REACH registration dossiers.

eREACHNano is a useful tool explaining REACH requirements for nanoforms. It guides companies (especially small and medium-sized companies) through the registration process for nanoforms and its requirements through e-learning modules.

CLP REGULATION

Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures (CLP Regulation) establishes criteria to identify hazardous substances and mixtures and to inform users (e.g., workers and consumers) regarding their hazards through standard symbols and phrases. CLP also sets out rules for packaging of hazardous chemical products. Manufacturers and importers need to notify the classification and labelling to ECHA when they place hazardous substances and mixtures on the EU market. CLP regulation does not have nanomaterial-specific provisions. Substances or mixtures that are composed of nanomaterials or contain special nanoforms, fulfilling the criteria for classification as hazardous under CLP Regulation must be classified and labelled. More details can be found here.

NANOMATERIALS IN THE REGULATION FOR COSMETIC PRODUCTS

The Cosmetics Regulation (EC) No. 1223/2009 specifically concerns nanomaterials in cosmetic products. If a cosmetic product contains nanomaterials, which is clearly defined in the Regulation, the person (e.g. manufacturer, importer or third party designated by such) responsible for the product shall send both general and nano-specific information to the European Commission via the Cosmetic Products Notification Portal CPNP six months before the product is released on the market. This does not, however, apply to materials used as dyes, UV filters or preservatives which are subject to a specific approval procedure.

If the Commission has concerns about the safety of the nanomaterial contained in the product, the Commission shall send a request to the Scientific Committee for Consumer Safety (SCCS), without delay, to issue an opinion on the safety of this nanomaterial for the relevant categories of cosmetic products and the reasonably foreseeable conditions regarding exposure. The Commission shall make this information public. The SCCS shall deliver its opinion within six months of the Commission's request. Should SCCS consider that any necessary information is missing, the Commission shall require the responsible person to provide this information within an expressly stated and reasonable time limit which may not be extended. SCCS shall deliver its final opinion within six months of the supplementary information being submitted. The statement from SCCS shall be made available to the public.

For nanomaterials that are not yet included in annexes III, IV, V or VI of the Cosmetic Products Regulation (i.e. have not yet undergone a full risk assessment by the SCCS), the responsible person shall provide the European Commission with at least the following information: i) identification of the nanomaterial; ii) the physical and chemical properties of the nanomaterial; iii) estimated annual amount of nanomaterials planned to be placed on the market through the cosmetic product; iv) the toxicological profile of the nanomaterial; v) reasonably foreseeable exposure conditions and vi) the safety data sheet for the nanomaterial and associated risk assessment. Taking into account the conclusion of the SCCS risk assessment, the European Commission may amend annexe II (list of substances prohibited in cosmetic products) and annexe III (list of substances that cosmetic products may contain only if specified restrictions are observed). Exceptions are cosmetic products that contain nanomaterials approved as dyes, UV filters or preservatives. These must be approved by the Member States who vote through amendments concerning the restriction of substances listed in the Annexes to the Regulation before they can be used in cosmetic products. All nanomaterials in the cosmetic product should be clearly indicated in the list of ingredients. The names of such components shall be followed by the word 'nano' in brackets.

Apart from the risk assessment which forms the basis for regulatory decisions, SCCS is also responsible for providing and updating the guidance for the safe use of nanomaterials in cosmetic products. For example, SCCS published Checklists for Applicants Submitting Dossiers on Cosmetic Ingredients, including a schematic outline for the safety assessment of nanomaterials and minimum information requirements of nanomaterials used in cosmetics, as well as the Guidance on the Safety Assessment of Nanomaterials in Cosmetics, (Guidance on the Safety Assessment of Nanomaterials in Cosmetics) and the latest version of the SCCS Notes of Guidance for the Testing of Cosmetic Ingredients and Their Safety Evaluation (Notes of Guidance for the Testing of Cosmetic Ingredients and Their Safety Evaluation).

BIOCIDAL PRODUCTS REGULATION

The Biocidal Products Regulation (EC) No 528/2012 (BPR) has specific provisions for nanomaterials. The provisions apply to products and substances that meet the criteria of nanomaterials defined in the BPR (the definition is based on the Commission Recommendation on the definition of a nanomaterial 2011/696/EU). All biocidal products and active substances should be evaluated separately, initiated from the dossier submission from the applicants to the competent authority in a chosen member state in the EU. The active substances contained in that biocidal product must be approved at the EU level prior to the authorization of the biocidal product at the national level. Some products (union authorizations) are authorized at the EU level.

However, the approval of the active substance does not cover the nanoform of the active substance except where explicitly mentioned. All data requirements in the application dossier must be fulfilled for nanomaterials of active substances. A thorough risk assessment should be provided separately when the nanoform of the active and non-active substances (e.g., formulants) are used in

a biocidal product. The label of the biocidal product must show the name of each nanomaterial followed by the word "nano" in brackets. Products containing nanomaterials are not eligible for simplified authorization procedure. MSCAs are responsible for the enforcement of BPR. Also, Member States must report on the implementation of the BPR every five years, which must include information on the use of nanomaterials in biocidal products and the potential risks identified. More information can be found here.

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NOVEL FOODS REGULATION

The General Food Law Regulation sets out an overarching framework for the development of food and feed legislation both at Union and national levels, covering all stages of food and feed production and distribution.

A food consisting of nanomaterials will be considered a novel food and as such will require authorization under the Novel Food Regulation (EU) 2015/2283, where "engineered nanomaterial" was clearly defined. Novel foods may only be placed on the market within the EU if they are authorized and are included in the Union list. The procedure for authorizing a novel food should start either on the Commission's initiative or following an application to the Commission by an applicant. The application should include: (i) the name and address of the applicant; (ii) the name and description of the novel food; (iii) the description of the production process(es); (iv) the detailed composition of the novel food; (v) scientific evidence demonstrating that the novel food does not pose a safety risk to human health; (vi) where appropriate, the analysis method(s); (vii) a proposal for the conditions of intended use and for specific labelling requirements which do not mislead the consumer or a verifiable justification why those elements are not necessary.

When nanomaterials are used, the applicants are supposed to provide explanation regarding the scientific appropriateness for the test method applied to nanomaterials and, where applicable, the technical adaptations or adjustments that have been made so as to respond to the specific characteristics of those materials. Then, the Commission may consult European Food Safety Authority (EFSA) on the suitability of the application and request EFSA to perform a human health risk assessment of the novel food within 9 months. Based on the scientific opinion of EFSA, the Commission shall submit a draft implementing act to the Standing Committee on Plants, Animals, Food and Feed (PAFF) authorizing the placing on the market of a novel food and updating the Union list. Food Information Regulation (EU) No 1169/2011 stipulates that all engineered nanomaterials in the novel food should be clearly indicated in the list of ingredients. The names of such ingredients shall be followed by the word 'nano' in brackets.

In addition to carrying out the risk assessment of novel food, EFSA is also responsible for verifying that the most up-to-date test methods have been used to assess their safety. Besides, EFSA provides guidance for applicants on the preparation and submission of an application for authorisation of a novel food, where nano-specific information requirements are available. Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: human and animal health, published by EFSA in 2021, provides an overview of additional or complementary information requirements specifically for nanomaterials and how to perform risk assessments of nanomaterials in the food and feed area. EFSA has also developed a Guidance on Technical Requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles, which complements the former guidance, defining the criteria for assessing the presence of a fraction of small particles, and setting out information requirements. Currently, EFSA does not provide guidance for Environmental Risk Assessment (ERA) of nanomaterials used in food and feed chain. However, a report published by EFSA compiles and structures the relevant information for ERA of nanomaterials, aiming for supporting the preparation of future guidance.

FOOD ADDITIVES REGULATION

All food additives in the EU must be authorised and listed with conditions of use in the EU's positive list (Community list) under the Food Additives Regulation (EC) No 1333/2008. To get food additives authorized, applicants are supposed to submit the application dossier to the Commission via Member States. The Commission may consult European Food Safety Authority (EFSA) on the suitability of the application and request EFSA to perform a risk assessment of the food additive. Based on the scientific opinion of EFSA, the Commission shall submit a draft implementing act to the Standing Committee on Plants, Animals, Food and Feed (PAFF) authorizing the placing on the market of a food additive and updating the Community list. Different from novel food, there is no nano-specific application procedure for food additives. However, when a food additive is already included in the Community list and there is a significant change in particle size through nanotechnology, this food additive should be considered as a different additive. Therefore, a new entry in the Community lists or a change in the specifications shall be required before it can be placed on the market. Food Information Regulation (EU) No 1169/2011 stipulates that all nanomaterials used as food additives should be clearly indicated in the list of ingredients. The names of such ingredients shall be followed by the word 'nano' in brackets.

In addition to carrying out the risk assessment of food additives, EFSA is also responsible for providing guidance for applicants on the preparation and submission of an application for authorisation of a food additive, where nano-specific information requirements are available. Guidance on risk assessment of nanomaterials to be applied in the food and feed chain: human and animal health, published by EFSA in 2021, provides an overview of additional or complementary information requirements specifically for nanomaterials and how to perform risk assessments of nanomaterials in the food and feed area. EFSA has also developed a Guidance on Technical Requirements for regulated food and feed product applications to establish the presence of small

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FOOD CONTACT MATERIALS REGULATION

Regulation (EC) 1935/2004 is a harmonized legal framework for the safety of Food Contact Materials (FCM). Regulation (EC) No 1895/2005 on the restriction of the use of certain epoxy derivatives in materials and articles intended to come into contact with food; Regulation (EC) No 2023/2006 on good manufacturing practice; Regulation (EC) No 282/2008 on recycled plastic materials and articles intended to come into contact with food; Regulation (EC) No 450/2009 on active and intelligent materials and articles intended to come into contact with food; Regulation (EU) No 10/2011 on plastic materials and articles intended to come into contact with food; Regulation 284/2011 on imports of polyamide and melamine plastic cookware from China and Hong Kong; and Regulation (EU) 2018/2013 on the use of bisphenol A in varnishes and finishes intended to come into contact with food were established under this framework.

Regulation (EU) No 10/2011 addresses the use of nanomaterials in plastic FCMs. It stipulates that substances in nanoform should only be used if explicitly authorised and mentioned in the specifications in Annex I. The Commission provides Union Guidance on Regulation (EU) No 10/2011 on plastic materials and articles intended to come into contact with food as regards information in the supply chain, aimed at European Professional Organisations and Member States competent authorities dealing with questions concerning the interpretation and implementation of certain aspects on the declaration of compliance and adequate information in the plastics supply chain, including nanomaterials.

Regulation (EC) No 450/2009 set out requirements of the use of nanomaterials in active and intelligent FCMs. When nanotechnologies were used, and substances exhibit physiochemical properties that significantly differ from those at a larger scale, the substances should be assessed on a case-by-case basis regarding their risk until more information is known about such new technology.

MEDICAL DEVICES REGULATION

Medical Devices Regulation (EC) No. 2017/745 (MDR) includes products that are not any form of medicine but are intended for medical purposes. There is a wide range of products in the field of medical devices, they may be everyday products such as plasters and condoms, substance-based products such as sprays and creams, aids for people with disabilities as well as advanced products

such as pacemakers and hospital equipment. In the European Union (EU) and the European Economic Area (EEA), they must undergo a conformity assessment to demonstrate they meet legal requirements to ensure that they are safe and perform as intended in accordance with the MDR regulation (Medical Device Reporting). It is the responsibility of the manufacturer to carry out this conformity assessment. When assessing the conformity of products belonging to the medium and high risk class, an independent party, a so-called notified body, shall participate in the conformity assessment and issue a certificate that is the basis for the manufacturer's final assessment. The notified body's review has a different scope based on the product's risk class.

The MDR is an EU regulation and thus applies directly throughout the EU and EEA. In a few areas, the MDR can be supplemented by national regulations. These areas do not apply to the general principles of safety and performance of the medical devices, for example the assessment of nanomaterials is a matter that may not be controlled nationally. The authorities in EU member states appoint and control the notified bodies that may participate in conformity assessments. In Sweden, the Medical Products Agency is responsible for appointing and controlling the notified bodies. For certain types of medical devices where substances are included, the notified body may consult a medicines agency as a part of its assessment, more information about this can be found on the following websites, Medical Products Agency and European Medicines Agency (EMA).

All substances and materials included in a medical device must be evaluated and assessed for safety and performance. The risks that are identified must first be eliminated, and then minimized and only risks that are acceptable in relation to the benefits for the patient may remain. The risk assessment must be constantly updated based on the product's use and the generally recognised scientific and technical stage of development. If nanomaterials, which are clearly defined in the regulation, are used in medical devices, manufacturers must take them into particular consideration in their evaluation and assessment. Medical devices must be designed and manufactured in such a way that the risks linked to the size and properties of the particles that are released or may be released into the patient's or user's body are reduced as far as possible, if the products do not come into contact only with intact skin. Products that contain or consist of nanomaterials are subject to a special rule for assigning a risk class, which in turn affects which conformity assessment procedure is applied. If the nanomaterial tends to trigger high or medium internal exposure, the products shall belong to class III and undergo the most stringent conformity assessment procedures. All medical devices that involve any risk of internal exposure to nanomaterials belong to a risk class that means that the notified body shall participate in the conformity assessment. International Organization for Standardization (ISO) provides guidance describing considerations for the biological evaluation of medical devices that are composed of or contain nanomaterials. In the "Guidance on the Determination of Potential Health Effects of Nanomaterials Used in Medical Devices" the Scientific Committee on Emerging and Newly Identified Health Risks (SCHENIHR) provides guidance on specific factors that need to be considered in the risk assessment of medical devices containing nanomaterials.

SWEDISH CHEMICALS REGULATION

In Sweden, national regulation KIFS 2017:7 on chemical products and biotechnological organisms (KIFS 2017:7 om kemiska produkter och biotekniska organismer) explicitly addresses nanomaterials at chapter 3, including i) definition of nanomaterials; ii) Notification obligation regarding certain chemical products with intentionally added nanomaterial; iii) exceptions for certain notifier and iv) information to be provided if the product contains nanomaterials.