Nanomaterials in Food – Current and Future Applications and Regulatory Aspects

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Abstract. Nanotechnology can contribute to the development of innovative applications in the agriculture, food and feed sector by e.g. enabling improved delivery of nutrients or increased efficacy of agrochemicals. It is expected that applications will increase in the near future and may therefore become a relevant source of human exposure to nanomaterials (NM). To gain more up-to-date information, RIKILT and the Joint Research Centre (JRC) were commissioned by the European Food Safety Authority (EFSA) to prepare an inventory of currently used and reasonably foreseen applications of NM in agriculture and food/feed production and carried out a review of regulatory aspects concerning NM in both EU and non-EU countries. An analysis of the information records in the inventory shows that nano-encapsulates, silver and titanium dioxide are the most frequent type of NM listed and that food additives and food contact materials are the most frequent types of application. A comparison between marketed applications and those in development indicates a trend from inorganic materials (e.g. silver) towards organic materials (nano-encapsulates, nanocomposites). Applications in novel food, feed additives, biocides and pesticides are currently mostly at a developmental stage. The review of EU and non-EU legislation shows that currently a few EU legal acts incorporate a definition of a nanomaterial and specific provisions for NM, whereas in many non-EU countries a broader approach is applied, which mainly builds on guidance for industry.

1. Introduction
Nanotechnology can contribute to the development of innovative applications in the agriculture, food and feed sector (hereinafter referred to as agri/feed/food) with new and enhanced properties [1, 2]. Applications include nano-encapsulated agrochemicals or nutrients, antimicrobial nanoparticles and active and intelligent food packaging. It is expected that applications will increase in the future and thereby represent a relevant source of direct exposure of humans to nanomaterials (NM). To address this potential concern and to gain more up-to-date information on the exposure potential to NM applied in agri/feed/food products, RIKILT and JRC have prepared for the European Food Safety

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2. Nano Inventory

Relevant information for the Nano Inventory was retrieved through an extensive literature search performed in bibliographic databases such as Scopus, Web of Science, PubMed Central, NANOnetBase and SciFinder Scholar, and complemented by ad-hoc searches in the internet, at company websites and through questionnaires sent to different stakeholders. The retrieved data and information were evaluated based on selection and exclusion criteria and, if considered relevant, inserted into the Nano Inventory. The Nano Inventory was developed in a Microsoft® Access environment and organised in 12 different application fields related to agri/feed/food (Figure 1). From the database, three predefined queries were developed to extract the most relevant data and information.

![Figure 1: Application fields in the Nano Inventory](image)

3. Current and future applications of nanotechnology in agri/feed/food

Most of the records in the Nano Inventory concern applications in food (almost 90%) with food additives and food contact materials being the most frequent types of application. A much smaller percentage of applications in the Nano Inventory is concerned with agriculture (9%) and feed (3%). 55 different types of NM, both inorganic and organic, can be found in the Nano Inventory. The most frequent types of NM are nano-encapsulates, silver and titanium dioxide (Figure 2).
About half of the identified applications are claimed to be already used in a consumer product while about 20% of the applications are still in the research and development stage. For the remaining applications the available information did now allow to determine the status.

A comparison between marketed and in development applications indicates a trend from inorganic materials (e.g. silver) towards organic materials (nano-encapsulates, nanocomposites) (Figure 3). Applications in novel food, feed additives, biocides and pesticides are currently mostly at a developmental stage.

Applications of NM in agriculture include improved and targeted pest management and crop protection through increased efficacy, durability, bioavailability and controlled release of pesticides and other agrochemicals [4]. This can for example be achieved by nano-encapsulation or binding active substances to solid lipid nanoparticles or porous solid particles (e.g. silica) [5, 6]. Nanotechnology can also enhance crop production and thereby potentially reduce the quantity of fertiliser that has to be applied [7]. Nanotechnology is also applied for detection of animal and plant pathogens, and for identity preservation and tracing and the slow release of nutrients or active compounds used in veterinary drugs [8, 9].
In food and feed processing, nanotechnology can contribute to new or improved tastes, textures and mouth sensations through nano-scale processing of foodstuffs or improved uptake, absorption, and bioavailability of nutrients through nanoscale-formulations [10]. Several food additives are composed of nanoparticles or may contain a fraction in the nanosized range. Synthetic amorphous silica (SAS) is used for surface coating of packaging materials, for the clearing of beverages, and mostly as a free-flow and anti-caking agent in many powdered food items (E551) [11]. It is composed of aggregates of primary particles of nanosize. Titanium dioxide which is mainly used as white pigment may contain also particles in the nanosize range.

Nanotechnology has contributed to the development of innovative packaging materials that can improve the safety and shelf life of products by providing barrier materials or detect foodborne pathogens. Some applications are already marketed while many more are at the moment in the research and development stage [1, 9].

4. Toxicological data and risk assessment

Data and information stored in the Nano Inventory indicate that silica, silver and titanium dioxide are the most common NM in toxicity testing and risk assessment. The most tested toxicity endpoints include genotoxicity, acute toxicity, cytotoxicity and repeated dose toxicity. Very often the physicochemical characterisation of the NM is very poor and was reported in less than 15% of the records concerning (eco)toxicity and risk assessment of NM.

5. Review of legislation addressing nanotechnology in agri/feed/food

To prepare the overview of existing legislation and guidance for risk assessment with regard to NM and nanotechnology in agri/feed/food in both EU and non-EU countries we collected information from websites of the European Commission, European Agencies/Authorities, the Official Journal of the European Union, national governments, and national and international organisations. In addition, we searched peer-reviewed publications as described above. Information on non-EU legislation was mainly retrieved from recently published reports, such as by WHO/FAO [12] or OECD [13]. In addition a questionnaire on "Regulation and safety assessment of nanomaterials in agri/feed/food applications" was sent to relevant stakeholders (RIKILT and JRC 2014).

The EU is the only world region where nano-specific provisions have been incorporated in legislation for agri/feed/food. Some EU legislations explicitly addressing NM include the Regulation on the Provision of Food Information to Consumers (1169/2011), the Regulation on Plastic Food Contact Materials and Articles (10/2011), the Regulation on Active and Intelligent Materials and Articles (450/2009), the Biocidal Products Regulation (528/2012) and the Cosmetic Products Regulation (1223/2009). In other sectors NM are considered implicitly covered by legislation [14]. Some pieces of legislation are currently under revision to better address NM, e.g. Novel Food Regulation (258/97) [15].

The use of nanotechnology in food production is currently covered by EC Regulation No 258/97 concerning 'novel foods' and 'novel food ingredients' [16] which addresses food not consumed to any significant degree in the EU prior to May 1997. The revised regulation will address NM and nanotechnology more explicitly by covering 'foods modified by new production processes such as nanotechnology and nanoscience and food or vitamins, minerals and other substances containing or consisting of 'engineered nanomaterials'. A pre-market approval (safety assessment and authorization) is required for novel food as well as for food additives. Food additives on the market before 2009 are subject to re-evaluation, during which potential nanospecific data can be considered [17]. This includes also some of the common particulate food/feed additives, which have been in use for years, such as anti-caking/free-flow powders, pigments and others (e.g. silicon dioxide, titanium dioxide, iron oxide or silver).

Countries outside the EU have rather adopted a broad approach when dealing with regulation of NM in agri/feed/food. Many non-EU countries have introduced non-mandatory frameworks and
consider existing regulatory frameworks able to adapt to and cover the particularities of NM (e.g. US, Australia and New Zealand, Canada). They rather build on guidance for industry.

In the EU some sectors have introduced a legally binding definition of the term 'nanomaterial' (i.e. for food, cosmetic and biocidal products). Furthermore, an EC Recommendation for a broadly applicable definition of 'nanomaterial' is available (2011/696/EU). All EU definitions of the term 'nanomaterial' intended for regulatory purposes use size (1-100 nm or below 100 nm) as main identifier. There are differences among the EU definitions with regard to inclusion criteria (e.g. only intentionally produced NM for food) or thresholds (e.g. number size distribution). An alignment of sector-specific definitions with the EC Recommendation is currently (January 2015) being discussed. No legally binding definitions could be identified outside EU and rather working definitions of NM are applied. Beside size some countries (e.g. US, Canada) consider also other properties or phenomena to define NMs or nanotechnology.

In the EU all ingredients present in food or biocidal products in the form of NM have to be clearly indicated in the list of ingredients with the names of such ingredients followed by the word 'nano' in brackets (Figure 4). A system for tracking and labelling consumer products containing NM has been introduced by some Asian countries such as Iran, Taiwan and Thailand (e.g. NanoMark system in Taiwan). This system is substantially different from the labelling requirement in the EU. While in EU the labelling of products containing nanomaterials is a mandatory requirement included in specific pieces of legislation (food, cosmetics and biocides legislations), the labelling introduced in the above mentioned non-EU countries is established within the context of "industrial standard certifications for nanoproducts" and it is aimed at eliminating fake nanoproducts on the market. Both finally aim to inform consumer and to protect their rights.

**Figure 4:** Example of labelling of a food product containing amorphous silicon dioxide (E551) in nanoform as anticaking agent.

**Ingredients:**
...

6. Conclusions
Nanotechnology applications in the agricultural, feed and food sector are growing and novel products are expected to enter the market in the near future. An up-to-date knowledge on the occurrence and type of application of NM in this sector is vital to estimate the potential human exposure to NM from food and feed. It is also becoming increasingly important that the regulatory frameworks properly address and specifically manage the potential risks of nanotechnology. Several countries over the world have been particularly active in examining the appropriateness of their regulatory frameworks for dealing with nanotechnologies but have applied different approaches to address safety issues of nano-based products in agri/feed/food: from legally binding provisions to guidance for industry.

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