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Regulatory challenges of nanomaterials in food and feed

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ABSTRACT

Nanomaterials, including engineered particles with dimensions in the nanoscale range (≤100 nm), are increasingly used in the food and feed sectors, particularly in applications such as nanoencapsulation of bioactive compounds, targeted nutrient delivery, texture improvement, and shelf-life extension. This study analyses the European Union's legal framework, including the 2011 and 2022 European Commission recommendations, Regulation (EC) No 178/2002, Regulation (EU) 2015/2283, and European Food Safety Authority (EFSA) guidance documents, and highlights definitional ambiguities and regulatory inconsistencies that hinder effective risk assessment and management. Ongoing debates concerning the 50% particle size threshold used to define a nanomaterial illustrate these challenges. Using a qualitative and comparative legal approach grounded in the precautionary principle and scientific uncertainty, the study identifies major gaps in current risk assessment, including issues related to particle accumulation, long-term exposure, and the lack of validated methods for characterisation and detection. Based on these findings, key regulatory improvements are proposed: clearer and harmonised definitions, updated classification thresholds, stronger requirements for data on physicochemical properties, and enhanced

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transparency in risk communication. These recommendations aim to inform the ongoing revision of EFSA guidance (2024–2029) and support the development of a coherent and effective regulatory framework for nanomaterials in food and feed.

KEYWORDS

engineered nanomaterials, food law, risk assessment, EFSA guidance, food safety, regulatory framework, nanotechnology in food

1. INTRODUCTION

Nanoparticles are fragments of matter with physical dimensions not exceeding 100 nanometres (nm) (Sing et al., 2017). Nanomaterials, including nanoparticles, are the focus of nanotechnology, which involves the design and creation of nanostructures applied in fields such as pharmaceuticals, medicine, cosmetics, and the food and feed industries. Food and feed may naturally contain components with internal structures existing at the nanoscale, such as naturally occurring molecules, micelles, or crystals (European Food Safety Authority - EFSA, 2009). Nanomaterials are increasingly being intentionally used in food and feed to improve properties such as taste, shelf life, nutrient bioavailability, or the stability of bioactive compounds, for example through the use of nanocapsules containing omega-3 fatty acids (Neme et al., 2021).

Research on nanoparticle structure has shown that their properties change with miniaturisation. Compared to their bulk counterparts, nanomaterials exhibit unique chemical and physical properties, particularly an increased ability to participate in chemical reactions due to their small particle size and larger surface-to-volume ratio (Sing et al., 2017).

Although some nanomaterials have been present in the food sector for decades, growing scientific concerns and new toxicological findings have led to bans on certain substances. A notable example is titanium dioxide (E171), a commonly used pigment, whose technological role was to enhance the colour and opacity of food products (Commission Regulation (EU) 2022/63). While not strictly a nanomaterial by definition, E171 was identified as a particulate mixture of micro- and nanoparticles, with a significant fraction below 100 nm (Younes et al., 2021). The presence of this nano-sized fraction, combined with its persistence in the body and potential genotoxicity, raised safety concerns. In May 2021, EFSA published a scientific opinion concluding that titanium dioxide can no longer be considered safe as a food additive, mainly due to unresolved uncertainties regarding its potential to cause DNA damage (Younes et al., 2021). Based on this assessment, the European Commission, together with EU Member States, adopted Regulation (EU) 2022/63, banning the use of titanium dioxide in food, with exceptions for certain medicinal products (Commission Regulation (EU) 2022/63).

A key challenge is the absence of a single comprehensive legal act in the EU regulating nanomaterials in food and feed. Instead, various provisions are dispersed across different regulations addressing novel foods (Regulation (EU) 2015/2283), food additives (Regulation (EC) 1333/2008), and food contact materials (Commission Regulation (EU) 10/2011). Regulation (EU) 2015/2283 defines "engineered nanomaterials," and the 2022 European Commission Recommendations set a percentage threshold of particles below 100 nm, above which materials are

classified as nanomaterials. Proposed changes have raised concerns and been criticised by the European Parliament (European Parliament resolution C(2024)01612 – 2024/2691(DEA)). From a legal perspective, the lack of a unified classification system leads to interpretive ambiguities and regulatory gaps. Additionally, limitations in risk assessment, particularly regarding bioavailability, tissue accumulation, and environmental persistence of nanomaterials complicate effective risk evaluation and compliance with EU food and feed safety standards.

According to Regulation (EC) 178/2002, the precautionary principle is not the primary factor in food safety assessment but should be applied when scientific evidence is insufficient or uncertain. This means food safety can only be ensured by fully understanding the properties of nanomaterials and their potential toxicity. Therefore, the food and feed sector requires a regulatory framework capable of rationally managing risks associated with nanotechnology, considering both health and environmental impacts.

The aim of this article is to analyse the European Parliament and Council regulations, European Commission recommendations, and EFSA guidelines, identifying areas requiring legal regulation—particularly regarding nanomaterials in food and feed. The legal framework will be evaluated through a model that ensures consumer safety in a rational and science-based manner.

2. MATERIALS AND METHODS

This article employs a qualitative comparative analysis method, focusing on the evolution of the definition of nanomaterials in key European Union documents, including Commission Recommendation 2011/696/EU of 18 October 2011 and its revision in Recommendation 2022/C 229/01 of 10 June 2022. The source materials also encompass relevant food law provisions, such as Regulation (EC) No 178/2002, Regulation (EU) 2015/2283 on novel foods and related implementing acts, as well as the EFSA Guidance on the risk assessment of nanoscience and nanotechnologies in the food and feed chain (2021) (More et al., 2021).

The evaluation of the 2022 definition of nanomaterials is conducted from the perspectives of the precautionary principle, scientific uncertainty, and its consistency with the risk analysis approach established in EU food law. Particular emphasis is placed on identifying classification criteria such as the percentage of particles within the 1–100 nm size range, volume-specific surface area (VSSA), and the exclusion of liquid and gaseous particles. The analysis further addresses the regulatory implications of the revised definition, including its impact on the scope of risk assessments and the practical application of food law.

The research method consisted of a systematic review and qualitative analysis of legal and scientific documents, without the use of quantitative data. Conclusions were drawn based on a structured assessment of the influence of the new definition on food safety, regulatory compliance, and practical oversight of products containing nanomaterials.

3. DISCUSSION

3.1. Changes in definition

One of the key legislative challenges in the regulation of nanotechnology is the definition of nanomaterials. Initially, the European Union's regulatory approach to nanotechnology was

shaped incrementally, in line with a stepwise regulatory philosophy. The European Commission advocated for addressing any potential risks associated with these innovative technologies within existing regulatory frameworks, which would be adapted over time in light of scientific developments. Furthermore, the Commission emphasised the importance of public dialogue and participatory governance in shaping such regulations (European Commission COM, 2004). This approach drew criticism from the scientific community and led, beginning in 2009, to the development of a comprehensive scientific definition of nanomaterials (Bleeker et al., 2012). A similar position was taken by the European Parliament, which, in its report on the regulatory aspects of nanotechnology, acknowledged the need for a coherent, science-based definition of nanomaterials. It also stressed that such a definition should be incorporated into both horizontal and sector-specific legislation, in order to account for the unique characteristics of nanomaterials (Directive 2009/128/EC; Bowman et al., 2010). Since then, legislative developments concerning nanomaterials have progressed primarily within sectoral regulations related to food and feed. As a result, the current legal framework addressing nanomaterials remains fragmented, with provisions scattered across various domains, including food additives, novel foods, food contact materials, and feed additives (Regulation (EC) 1333/2008; Regulation (EU) 2015/2283; Commission Regulation (EU) 10/2011). For manufacturers developing innovative food formulations, such as nanoformulations or encapsulation of active substances, the legal definition set forth in Article 3(2)(f) of Regulation (EU) 2015/2283 on novel foods is of particular importance. This provision defines engineered nanomaterials as: "any intentionally produced material that has one or more dimensions of the order of 100 nm or less or that is composed of discrete functional parts, either internally or at the surface, many of which have one or more dimensions of the order of 100 nm or less, including structures, agglomerates or aggregates which may have a size above the order of 100 nm but retain properties that are characteristic of the nanoscale" (Regulation (EU) 2015/2283). This definition is critical because it implies that any novel food containing engineered nanomaterials must undergo mandatory EU-level pre-market authorisation. To date, only one product listed in the Union list of authorised novel foods (Regulation (EC) No 1831/2003), established under Regulation (EU) 2015/2283, is explicitly classified as an engineered nanomaterial: iron hydroxide adipate tartrate (IHAT), a compound developed using nanotechnology to enhance iron bioavailability while minimising adverse effects. The definition of a nanomaterial provided in the Novel Food Regulation explicitly refers to "engineered" materials and does not set a quantitative threshold for the particle size distribution below 100 nm. Both Regulation (EU) 2015/2283 and Regulation (EU) 1169/2011 on the provision of food information to consumers adopt the same definitional approach: the mere presence of nanoscale particles is sufficient for a substance to be classified as a nanomaterial, without specifying a numerical particle-size threshold. In contrast, Regulation (EC) No 1333/2008 on food additives does not provide its own definition of nanomaterials. However, Article 12 of that regulation determines that any application of particle-size modifying technologies (such as nanotechnology) requires re-evaluation and authorisation of the additive. Similarly, Regulation (EC) No 1831/2003 on feed additives does not explicitly define "nanomaterials", yet any new substance or modified form, including nanoforms, must undergo a separate safety assessment. This means that the applicability of the "engineered nanomaterial" definition across various pieces of legislation depends on whether a given regulation explicitly adopts or refers to this definition, or does so implicitly in a specific context.

Importantly, the definition of an engineered nanomaterial set out in the Novel Food Regulation (EU) 2015/2283 does not establish a specific numerical threshold for the proportion of particles with dimensions below 100 nm, above which a material would be classified as a nanomaterial. To address this regulatory gap, the European Commission issued non-binding Recommendations in 2011 and 2022 on the definition of "nanomaterial" for legislative purposes. Notably, these Recommendations concern a general definition of nanomaterial and are not limited to materials intentionally produced through engineering processes (i.e., engineered nanomaterials). This approach is justified by the fact that the situation becomes more complex in the case of conventional materials, which do not meet the definition of engineered nanomaterials but may nonetheless contain small particles, including those within the nanoscale range (<100 nm in one or more dimensions). A typical example is novel foods consisting of complex mixtures, such as plant extracts, postbiotics, or microalgae, which may contain nanoscale fractions not intentionally introduced, but instead formed naturally or as incidental by-products during production, processing or formulation (Commission Implementing Regulation (EU) 2017/2470). Although the Commission Recommendations do not have legally binding status under EU law, they carry significant legal weight, as they serve as a key point of reference for incorporating nanomaterial definitions into sector-specific legislation and aligning regulatory approaches across different policy domains.

3.2. Updated EU definition of nanomaterials (2022)

The European Commission revised the previous definition of nanomaterial on June 10, 2022 (Commission Recommendation (2022/C 229/01)). The changes considered scientific and technological progress in this matter during last 10-year period. The 50% content of nanoparticles in the solid material was proposed as the threshold (Table 1). The definition of nanomaterial was revised by the European Commission on June 10, 2022 (Commission Recommendation (2022/C 229/01)), updating the original 2011 Recommendation (Commission Recommendation (2011/696/EU)). This revision was not only a response to scientific progress but also part of a scheduled review process explicitly foreseen in the 2011 text, which stated that the definition would be re-evaluated by 2014 based on experience and new scientific or technological insights. As part of this review, it was first of all necessary to determine whether the threshold size of the number size distribution of 50% should be increased or decreased, which formed a crucial element in reassessing the scientific basis and practical applicability of the definition.

Comparing the 2011 and 2022 recommendations, three key differences stand out:

1. The 2022 definition clarifies that nanomaterials consist of solid particles, as experts argued that unstable particles (i.e., liquid and gaseous) should be excluded.
2. The 2022 definition changes the approach to the problem described in the opinion of the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR, 2010). As a result, instead of explicitly include fullerenes, graphene flakes, and single wall carbon nanotubes with one or more external dimensions below 1 nm, the 2022 EC recommendations drop this inclusion and replace it with a general inclusion of all elongated particles (Rauscher et al., 2023).
3. Another change in the 2022 EU recommendation also excludes materials with a volume specific surface area (VSSA) of less than 6 m^2 cm^{-3} from the nanomaterials (Commission Recommendation, (2022/C 229/01)).

Table 1. Comparison of the 2011 and 2022 definitions of a nanomaterial, based on the Commission Recommendations of October 2011 (2011/696/EU) and June 2022 (2022/C 229/1)

2011 (2011/696/EU)	2022 (2022/C 229/1)
According to the 2011 European Commission definition, a "nanomaterial" is understood as a natural, incidental, or manufactured material containing particles in a free state, or in the form of an aggregate or agglomerate, where at least 50% or more of the particles in the number-based size distribution have one or more dimensions within the range of 1–100 nm	In the 2022 European Commission Recommendation, the definition was updated to specify that a nanomaterial is: A material consisting of solid particles, which occur individually or as identifiable constituent particles in aggregates or agglomerates In this material, 50% or more of the particles in the number-based size distribution must meet at least one of the following conditions: 1. One or more external dimensions of the particle fall within the size range of 1–100 nm ∘ Exception: Fullerenes, graphene flakes, and single-walled carbon nanotubes with at least one external dimension below 1 nm are also classified as nanomaterials 2. The particle has an elongated shape (such as a rod, fiber, or tube), where two external dimensions are smaller than 1 nm, while the third dimension exceeds 100 nm 3. The particle has a plate-like shape, where one external dimension is smaller than 1 nm, while the other dimensions exceed 100 nm
In specific cases, justified by environmental protection, health, safety, or competitiveness concerns, the threshold value for the number-based particle size distribution of 50% may be adjusted to a value within the 1–50% range	When determining the number-based size distribution of solid particles, it is not necessary to consider particles with at least two orthogonal external dimensions greater than 100 µm However, a material with VSSA less than 6 m^2 cm^{-3} is not considered a nanomaterial

It is worth emphasising that the revised definition of a nanomaterial, as provided in the European Commission's 2022 Recommendation (2022/C 229/01), maintains the 50% threshold, that is, a material is considered a nanomaterial if at least 50% of the constituent particles (by number) have one or more external dimensions in the size range of 1–100 nm. This threshold has been subject to criticism. Both the European Parliament and the EFSA have proposed lowering the threshold to 10%, advocating a more precautionary approach that takes into account potential health risks associated with low-level exposure to nanoscale particles (European Parliament *P9_TA(2024)0316*, EFSA Working Group Meeting on Nanotechnologies, 2024). As a result, there is currently a lack of harmonisation in the legal definition of nanomaterials, particularly in the area of food law, where existing legislation has yet to fully become consistent with the revised criteria established in the 2022 Recommendation (Commission Recommendation (2022/C 229/01)).

3.3. Precautionary principle

The precautionary principle has gained growing significance in EU policy making, particularly in response to public health concerns such as those that emerged during the BSE (Bovine Spongiform Encephalopathy) crisis. The precautionary principle is detailed in Article 191(2) of the Treaty on the Functioning of the European Union (TFEU) (Consolidated version of the Treaty on the Functioning of the European Union, Article 191, 2016). Although originally rooted in environmental protection, its scope has expanded over time to include broader areas such as food safety and consumer protection. The European Commission's 2000 Communication on the precautionary principle defines it as a risk management tool to be applied when a phenomenon, product, or process may pose a potential threat to human, animal, or environmental health, but scientific evidence remains inconclusive (Explanatory Memorandum to COM(2000)1 - Precautionary principle). In such situations, precautionary measures may be adopted to mitigate potential risks, provided these measures are proportionate, non-discriminatory, and subject to future review in light of new scientific developments. This approach has been reflected in various areas of EU legislation, including the regulations on food and feed. It acknowledges that achieving absolute certainty or a "zero-risk" scenario is unrealistic. Therefore, when there is scientific uncertainty regarding a potential hazard, precautionary actions may be implemented even in the absence of complete data.

Scientific uncertainty often arises from methodological limitations. It is typically associated with several key aspects of scientific evaluation, including the selection of variables, the measurements taken, the sampling techniques applied, the models used, and the underlying assumptions about causal relationships. Additional sources of uncertainty include data conversion errors, incomplete or missing data, and limitations in both qualitative and quantitative analyses such as the limit of detection (LOD) of a given analytical method.

This is particularly relevant to commonly applied nanomaterial characterisation techniques such as scanning electron microscopy (SEM), transmission electron microscopy (TEM), and dynamic light scattering (DLS). While these methods offer high-resolution imaging or particle sizing capabilities, they are not suitable for quantitatively determining the proportion of particles in the 1–100 nm range within complex food matrices, such as plant extracts, dairy emulsions, protein suspensions, or lipid-based formulations. These techniques are frequently affected by analytical artefacts, signal interference, and interpretative subjectivity, which collectively increase the level of uncertainty and hinder the fulfilment of EU regulatory requirements concerning nanomaterial classification. The practical misalignment between EFSA's theoretical guidance and real-world analytical capacity, as reported by stakeholders and applicants, underscores the urgent need to develop and validate methods that are both scientifically robust and tailored to actual product compositions (Rouault, 2025). This reinforces the importance of applying a structured and proportionate interpretation of the precautionary principle, enabling a high level of consumer and environmental protection even in cases of scientific uncertainty or evolving evidence.

3.4. Risk analysis

Legal measures ensuring food safety should be based on risk analysis conducted in an independent, objective, and transparent manner, using available information and data to assess potential hazards. This process allows scientific advisory bodies to estimate potential health risks,

particularly those associated with food products, technology of plant and animal production, hygiene conditions, etc., to protect human health and minimise the occurrence of diseases (FAO/WHO 2006).

The term risk analysis refers to a three-component process consisting of risk evaluation, risk management, and risk communication. According to the definition in Regulation (EC) 178/2002, these three components provide a systematic methodology for determining effective, proportionate, and targeted measures or actions aimed at protecting public health (Fig. 1).

The most crucial aspect of risk assessment is recognition of the hazard and determining the likelihood of its realisation. Therefore, risk assessment is a scientifically grounded process consisting of four key elements: hazard identification, hazard characterisation, exposure assessment, and risk characterisation (FAO/WHO 2006). When assessing exposure, it is essential to consider that the nano form of a given substance often exhibits different properties and may pose a significantly greater risk to human health and the environment than the same substance in its micro form. In the case of nanomaterials, like other chemical substances, there are four main exposure pathways: they can enter the body through inhalation, ingestion, skin absorption, or parenteral routes. Exposure can be more accurately characterised if the routes of entry, the physicochemical properties of the nanomaterials under study, the duration and frequency of exposure, as well as the amount of the nanomaterial involved are known (EFSA Scientific Committee, 2018). In the context of nanomaterials, effective risk management requires the consideration of both quantitative and qualitative uncertainties, which should be systematically integrated into the scientific assessment and decision-making process (EFSA Scientific Committee, 2011). The next step is identifying and characterising the hazards associated with nanomaterials. This is achieved through *in vitro* testing and computer simulations, which help detect adverse biological properties. To identify and characterise toxicological hazards, both *in vitro* and *in vivo* tests should be performed. The EFSA guidelines provide a structured approach to nanomaterial testing, which is based on four distinct stages (Commission Recommendation, 2022/C 229/01).

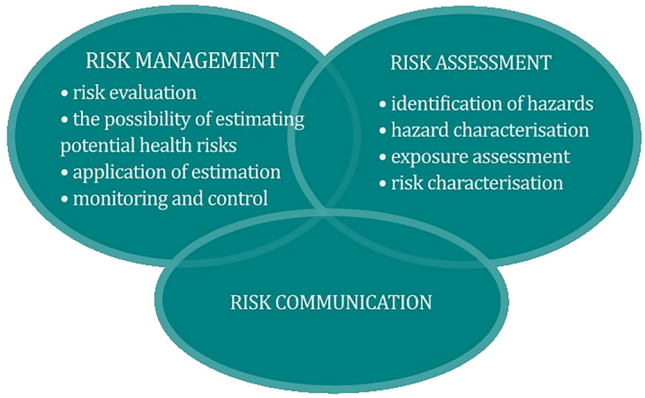

Fig. 1. Risk analysis framework according to the Food and Agriculture Organization (FAO) and the World Health Organization (FAO/WHO, 1995), illustrating (with modifications) the process consisting of risk assessment, risk management, and risk communication

1. In the first stage, the conversion rate of the nanomaterial into its non-nanomaterial form under conditions characteristic of the gastrointestinal tract must be examined. The purpose of this study is to identify materials that can be assessed according to the methodology for non-nanomaterials. EFSA must examine the rate of degradation of a nano-material to a non-nanomaterial under conditions representative of the gastrointestinal tract. Rapidly and completely dissolving nanomaterials can be subjected to conventional (non-nanomaterial) assessment instead of further nanospecific testing.
2. In the second stage, all available information should be gathered, and a series of *in vitro* studies should be conducted to identify potential hazards and determine whether further research is necessary. The stage involves assessing specific endpoints relevant to *in vitro* studies, including cytotoxicity/cell viability, induction of oxidative stress, (pro-)inflammation, and impairment of the gastrointestinal barrier integrity. Genotoxicity studies of nanomaterials should comply with the general EFSA genotoxicity testing strategy (Stirling et al., 1999), taking into account the specific properties of nanomaterials as described in these guidelines.
3. In the third stage, if a nanomaterial exhibits toxicity or persists in the organism, *in vivo* testing must be conducted, including a 90-day oral toxicity study in accordance with OECD Test Guideline No. 408, adapted for the specific assessment of nanomaterials. The purpose of such testing is to identify potential immunological, proliferative, neurotoxic, organ-specific, or endocrine effects. An ongoing revision of OECD testing guidelines is currently under discussion, which proposes to expand the range of endpoints to include these parameters, as well as the assessment of nanomaterial accumulation in tissues and their biological persistence (González, 2025).
   This knowledge is also very important from the point of view of the consumers of food descending from the animals fed diets supplemented with nanoparticles. To date, there is no analytical method that would allow the determination of the amount of nanoparticles, such as zinc, in meat, milk, or eggs. The other question is how long nanoparticles can persist in food of animal origin. If nanoparticles represent an unacceptable risk to the consumer, the withdrawal time/period should be established for those additives. Validated analytical methods for the detection and characterisation of nanomaterials in food and feed are being developed and made available, among others, by the Joint Research Centre of the European Commission (European Commission, Joint Research Centre, 2025) and as part of initiatives such as NanoHarmony.
4. In the fourth stage, if the results of the 90-day toxicity study indicate nanomaterial accumulation in tissues, the necessity of performing further detailed studies may be identified. These may include biodistribution in the human body, additional toxicokinetic studies, reproductive and developmental toxicity, additional immunotoxicity, neurotoxicity, mutagenicity, carcinogenicity, endocrine effects, and impacts on the gut microbiome.

Only after conducting all these studies, the risk associated with alimentary nanomaterials would be properly assessed. Risk characterisation integrates all information from hazard characterisation, exposure assessment, and any other relevant data. The outcome of risk characterisation should be a comprehensive safety assessment of the nanomaterial in relation to its intended use in food or feed. Only a thorough analysis of oral exposure and hazards posed by specific nanomaterials allows for a complete and scientifically based risk assessment.

There are also other aspects of nanomaterials. One of the problems that may occur is the safety of people who work with nanoparticles during the preparation of food and feedstuff. Routinely, the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) requires analysis of particle size by laser diffraction, test of dusting potential, and studies on skin sensitivity, and, if necessary, test for eye irritability of feed additives. Nanoparticles, because of their size, $P < 5$ µm may be inhaled deeply by the users to the pulmonary alveoli (More et al., 2021). Hence, the safety/health of the workers of food/feed industry and of farmers may be challenged if proper protection means are not applied. At this point, another question arises: are such protection means against nanoparticles available?

From a scientific perspective, the effectiveness of the introduction of appropriate requirements with regards to food and feed safety controls also affects environmental safety issues, although it is not obvious from a legislative point of view. Digestibility and bioavailability of nanoparticles are important not only for consumer and animal/target species safety evaluation. Nanoparticles that are not absorbed will be excreted in faeces, those absorbed might be excreted intact in urine or in bile if not metabolised. Animal manure is considered to be the perfect fertiliser, and if it contains nanoparticles, they will reach first the soil, secondly the plants, and thirdly the underground waters. Human excreta will finally reach the rivers and seas. If the bioavailability of nanoparticles is 100%, there will be no risk for the environment. In any other case, we can expect that nanoparticles will appear in the environment. The problem is how to study and calculate, for example, the half-life of nanoparticles in the environment. To our best knowledge, there are no reliable methods/models to study the life chain of nanoparticles and other food/feed additives in the environment. The 2024 EFSA guidelines introduce more detailed requirements for the design and documentation of feed additive efficacy studies. EFSA expects that data will be available for auditing and validation, and any methodological limitations should be disclosed (Bampidis et al., 2024).

3.5. Scientific uncertainty

The issue of scientific uncertainty is complex and has been recognised for a long time. As early as 25 years ago, the European Commission initiated the project "In the Management of Technological Risk" (Stirling et al., 1999). When assessing risks in food and feed, scientists identified several uncertainty factors that should be considered when developing regulations. In the case of nanotechnology, uncertainty can be reduced by using well-characterised nano-materials, ensuring that the form in which they are tested—whether in food, feed, or liquid matrices in animal studies—closely mimics the form expected in actual or existing food/feed products.

The EFSA Scientific Committee has outlined general principles and recommendations for identifying uncertainties in dietary exposure assessment, including data sources, criteria for data inclusion/exclusion, confidentiality, assumptions, and uncertainties. According to these principles, potential sources and types of uncertainty in nanomaterial exposure assessment should be systematically examined. Table 2 presents key areas of uncertainty regarding nanomaterials. In light of incomplete empirical data, the absence of harm cannot be presumed, which further justifies the legislative reliance on the precautionary principle.

Understanding uncertainty and its sources would help us to act better in the face of uncertainty, e.g., in political or scientific decisions related to research prioritisation or regulation (Heidmann and Milde, 2013).

Table 2. Key areas of uncertainty regarding nanomaterials

	Micro	Nano	Solutions
Toxicokinetics and toxicology	Toxicity testing methods (e.g., OECD test guidelines)	Testing methods that were not specifically designed for nanomaterials	Standard test protocols have not yet been adapted for testing nanomaterials, although work is ongoing, and additional OECD test guidelines are expected in the coming years
		There may also be additional toxic effects caused by nanomaterials that cannot be easily detected using current standard protocols	Additional endpoints (e.g., cardiovascular or immune function endpoints), which are not routinely considered, may need to be taken into account alongside traditional endpoints
Biochemical reactions	Biochemical reactions take place at the molecular level	Biochemical reactions occur at the molecular level on the surface of the nanomaterial with biological fluids, cell membranes Biochemical reactions take place at the molecular level, and cellular compartments	Answer to the question of what kind of biochemical or catalytic reactions take place on the surface of a nanomaterial
Allergies	Routine allergy testing for food ingredients	In the case of nanomaterials, comparison with existing allergenic proteins does not seem appropriate	Monitoring after a product has been released can also provide useful information

4. CONCLUSIONS

Regulations governing nanomaterials in food and feed pose significant legal and scientific challenges, primarily due to the evolving nature of nanotechnology and the inherent scientific uncertainties associated therewith. The fragmented and sectoral structure of the current EU regulatory framework, including provisions on food additives, novel foods, food contact materials, and feed additives, lacks harmonised definitions and uniform thresholds, particularly regarding particle size distribution and the presence of nanoscale fractions. The European Commission Recommendation of 2022 (2022/C 229/01) constituted a significant step towards redefining nanomaterials based on updated scientific evidence. However, the retention of the 50% threshold for particle size (1–100 nm) has sparked ongoing debate, with institutions such as the European Parliament and EFSA advocating for a more precautionary 10% threshold.

From a legal perspective, the absence of a clear classification system for nanomaterials, especially within complex matrices or materials not intentionally engineered as nanomaterials, gives rise to interpretative ambiguities and regulatory gaps. Moreover, limitations inherent to current analytical methods (e.g., SEM, TEM, DLS) impede precise quantification of nanoparticles, thereby complicating effective risk assessment and compliance with EU safety standards.

Scientific uncertainty remains an unavoidable element of nanomaterial risk analysis, particularly with respect to bioavailability, tissue accumulation, and environmental persistence. The lack of validated models to determine environmental fate and long-term effects of exposure to nanoformulated compounds, especially in the context of animal-derived food and manure recycling in agriculture, further complicates risk evaluation.

Accordingly, the precautionary principle, established in Article 191(2) TFEU and implemented across various food safety regulations, remains an indispensable legal instrument in scenarios characterised by scientific uncertainty.

Given these challenges, the present analysis highlights the need for regulatory action that not only resolves existing inconsistencies but also strengthens future regulatory oversight of risks/management. In this context, EFSA's guidance plays a key role as a soft law instrument, supporting the legal framework by providing practical tools for risk assessment. Strengthening regulatory coherence will require focused legislative and policy efforts, including:

a. Harmonising definitions and thresholds across all relevant EU legislation, with explicit consideration of the revised 2022 definition of nanomaterials.
b. Clarifying the regulatory status of unprocessed nanomaterials, including incidental nanoscale fractions present in complex food products such as plant extracts and probiotics.
c. Developing validated analytical methodologies enabling reliable detection and characterisation of nanoparticles in food and feed.
d. Implementing structured procedural frameworks to address scientific uncertainty, incorporating guidelines on data gaps, exposure modelling, and cumulative risk assessment.
e. Furthermore, forthcoming updates to EFSA's scientific guidance (2024–2029), including integration of methodologies and sector-specific assessment procedures, are anticipated to play a pivotal role in risk evaluation.

This analysis indicates that the current regulatory framework is no longer sufficient to keep pace with technological developments or the complexity of new nanotechnology applications in the food and feed sector. A more forward-looking, proactive approach is needed, which will not only resolve existing inconsistencies but also establish clear institutional responsibilities and a long-term legislative direction. These changes are necessary to ensure that regulatory mechanisms evolve in parallel with scientific progress and remain capable of protecting consumer and animal health.

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