17
Evolving Best Practice in Governance Policy – Developing Consumer Confidence in Risk Analysis Applied to Emerging Technologies

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17.1
Introduction

Risk governance is an important element that needs to be addressed following the development and identification of any new technology, including agri-food nanotechnology. Following a general introduction to the principles and components of the internationally acknowledged approach to food risk analysis, this chapter further discusses the "risk cycle" approach proposed by the European Union's Scientific Steering Committee. Risk analysis is supposed to bring together three interrelated risk-focused activities, comprising risk assessment, risk management, and risk communication. The European SAFE FOODS project has further devised amendments to these models for risk analysis, which have culminated in a newly developed integrated risk analysis framework. This framework considers risk analysis as an iterative, cyclic process that passes through four stages: framing, risk–benefit assessment, evaluation, and risk management. New elements contained by the integrated SAFE FOODS risk analysis framework include the increased emphasis on – and individuation of – the stages of framing and evaluation, at which the risk assessors and risk managers interact with each other and where also stakeholders can provide useful inputs and feedback. In addition, it is proposed that the risk assessment stage focuses not only on risks but also on other impacts, including human health benefits, as well as social, economic, environmental, and ethical impacts.

Risk management includes decision-making, implementation, and monitoring, after which review of the effectiveness of risk management can take place, possibly providing outcomes that feed back into the framing phase so that the cycle can start again. In general terms, increased stakeholder involvement, communication, and transparency are advocated throughout the risk analysis process.

An area in which the new integrated SAFE FOODS risk analysis framework could be relevant is that of nanotechnologies applied to food production and handling. This new technology holds great potential but can, at the same time, also pose new risks previously not encountered. The term "nanotechnology" actually covers a wide range of technological applications, which share the character-

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istics of nanometer-scale size structures as functional units. The properties of nanomaterials can differ greatly from the generic properties of the same materials (i.e., those which are larger than nano-size). As a consequence, potential toxic effects cannot be predicted because of lack of extrapolation. In line with the new integrated risk analysis framework, proposals are made regarding the identification and prioritization of areas for future research in the area of nanotechnology applied to agriculture and food production.

17.2
Introduction to Food Safety Governance

17.2.1
General Principles of Risk Analysis

Governance of food safety is conducted by most governments through application of the *risk analysis framework*, which is the dominant model applied in the area of regulation associated with food safety. International harmonization of food safety regulations is being conducted through the Codex Alimentarius, an organization co-founded by two United Nations organizations: the Food and Agriculture Organization (FAO) and the World Health Organization (WHO).

According to the general principles developed within Codex Alimentarius, the risk analysis framework can be separated into three distinct interrelated activities – risk assessment, risk management, and risk communication.

17.2.1.1 Risk Assessment

Risk assessment is performed by technical risk assessors. In some institutional contexts – for example, the European Food Safety Authority (EFSA) – there is a structural separation between risk management and risk assessment, although such institutional compartmentalization does not always apply – for example, the British Food Standards Agency (FSA) has responsibility for assessment, management, and communication within its terms of reference. Indeed, some stakeholders have criticized the structural and functional separation of risk assessment and risk management as non-pragmatic [2].

The process of risk assessment in the context of food safety was largely defined in a joint expert meeting convened by FAO/WHO [3], and four components were distinguished, namely (i) hazard identification, (ii) hazard characterization, (iii) exposure assessment, and (iv) risk characterization (see Figure 17.1). Hazard identification is the identification of a substance or attribute of food that may potentially cause adverse effects on human health. Whether such adverse health effects will occur depends on the exposure to the hazard. Within risk assessment, this is determined by studies on dose–response relationships between the hazard and the harmful effects in the target organs (the hazard characterization step), the

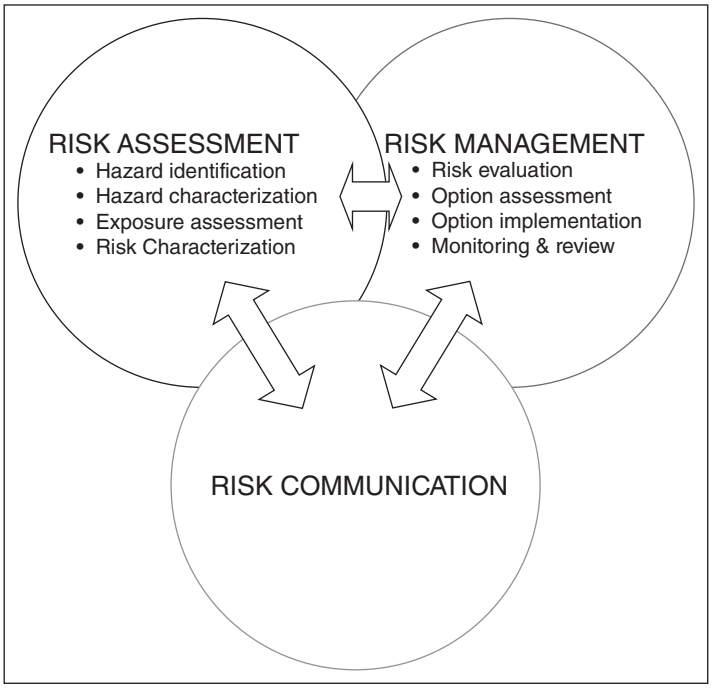

Figure 17.1 Risk analysis framework [1].

actual exposure of humans to this hazard (exposure assessment), and the risk of becoming exposed to levels of concern (risk characterization). The risk is determined as the product of the likelihood of the occurrence of the harm and the magnitude or severity of the effect.

17.2.1.2 **Risk Management**

Risk management is the decision-making process performed by risk managers in which the outcome of the risk assessment is weighed against other relevant data, and, if judged appropriate, prevention or mitigation measures are selected and implemented. Risk management generally initiates and ends the risk analysis process, and is composed of a number of elements: (i) risk evaluation (i.e., identification of food safety problem, establishing of a risk profile, ranking the hazard for risk assessment and risk management prioritization, establishing risk assessment policy, commissioning of risk assessment, and consideration of risk assessment results); (ii) risk management option assessment (i.e., identification of available management options, selection of preferred management options, and final management decision); (iii) implementation of management decisions; and (iv) monitoring and review (i.e., assessment of effectiveness of measures taken, and review of management and/or assessment as necessary) [4].

To initiate a risk assessment, the risk manager will prepare a "risk profile" by consulting all parties interested that are likely to be affected by the risk manager's decision. Once it has been decided to perform a risk assessment, this activity may be outsourced to independent risk assessors. In addition to safety, the risk manager may consider other factors as part of the risk assessment, such as the potential social, ethical, and economic impacts of the hazard or, indeed, hazard prevention or mitigation.

17.2.1.3 **Risk Communication**

Risk communication has been defined as the interactive exchange of information and opinions concerning risk and risk management activities among risk assessors, risk managers, consumers, and other interested parties [1]. It is assumed that interactive communication among all interested stakeholders, such as risk assessors, risk managers, industry, non-governmental organizations, primary producers, and consumers, *inter alia*, will assure transparency, facilitate the development of consistent decision-making, and improve the quality of decisions made.

17.2.2
Risk Analysis in Europe–the European Commission's Scientific Steering Committee Model

The advice to the European Commission regarding consumer health and food safety has previously been provided via its Directorate-General for Health and Consumers by a Scientific Steering Committee (SSC) and additional Scientific Expert Committees. This role is currently fulfilled by the European Food Safety Authority (EFSA). The mandate of these advisory bodies is to provide the European Commission with scientific advice or opinions about scientific and technical issues in their respective field of expertise and is based on the principles of "excellence", "independence", and "transparency". In 2000, a dedicated Working Group of the SSC published recommendations to harmonize risk assessment procedures between the various Scientific Advisory Committees [5]. The primary goal of this activity was to harmonize definitions and procedures among the various Scientific Advisory Committees, as well as to describe the underlying principles and to stimulate consistency, transparency, and quantitative approaches of the assessments.

The report also considers the "risk cycle" (see Figure 17.2), showing the various stages in the risk analysis framework, and builds further on the framework proposed by the experts consulted by FAO/WHO [1]. In a second report [6], further improvements to risk assessment were proposed, addressing, *inter alia*, issues such as the use of probabilistic modeling, the impact of emerging technologies on the risk assessment process, and the assessment of the impact on quality of life, including individual experience of quality-of-life parameters. The ultimate goal is maximizing health and well-being (considering potential impacts on human, animal, and environmental targets) as well as the quality of life experienced. This

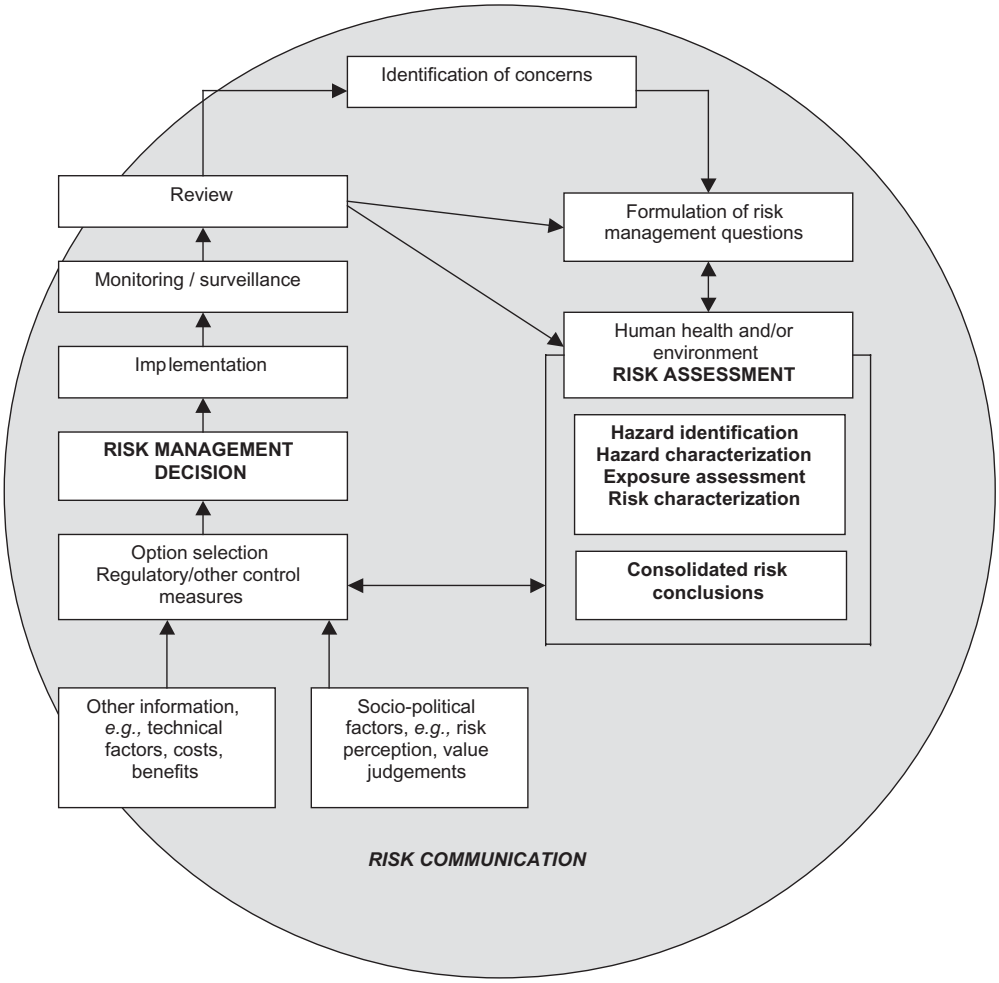

Figure 17.2 The "risk cycle" with components of risk analysis according to the EU Scientific Steering Committee [5].

is, of course, a remit reaching beyond the minimization of human health risks, requiring additional methodologies for collection of data on which decisions can be based.

The framing of appropriate questions by the Commission services is often the trigger for a new risk assessment. It is emphasized that a dialog between risk managers and risk assessors is important to achieve clear and achievable questions and should include the development of risk profiles of the putative hazard. It is also recognized that involvement of stakeholders in profiling the risk (e.g., identification of the criteria to be used, the specific issues to be addressed, and major concerns) will contribute to a more transparent and consistent risk assessment.

To facilitate improved transparency and acceptability of management decisions, all sources of data that have been used should be provided, including any limitations regarding the accessibility of potential data, the weighting of different datasets, and whether or not stakeholders have the opportunity to submit additional data. Additional improvement of the risk analysis framework will be achieved if risk assessors and relevant stakeholders are involved in the analysis.

17.3 Potential Innovations to the Risk Analysis Framework as Proposed by SAFE FOODS

17.3.1 The SAFE FOODS Project

Funded through the European Union's (EU) Sixth Framework Program, the four-year project "Promoting Food Safety Through a New Integrated Risk Analysis Approach for Foods" (known as SAFE FOODS) commenced its activities in 2004. The research has attempted to integrate natural and social science research activities, and involves 37 institutions from 21 countries (including non-European institutions in China, South Africa, and Russia). As an overarching objective, this project aimed to contribute to strengthening consumer trust in the food safety governance in Europe and beyond.

The research performed within SAFE FOODS attempted to improve current risk analysis practices for foods produced by different breeding approaches and production practices deploying high- and low-input systems. As one of the main outputs of this project, an "improved risk analysis framework" has been developed, which is underpinned by new scientific assessment methods, and embedded in a broad impact analysis of social, financial, and economic consequences, and with high levels of transparency, active public engagement, and improved risk communication. In addition, practitioners working in the field of food safety governance and other relevant stakeholders were consulted to maximize the applicability and acceptability of the framework.

The research was conducted in a number of interdependent projects, which delivered the elements for the construction of the improved risk analysis framework. The project's strategic objectives were the following.

- To design a European working procedure for early identification of emerging chemical or microbial risks in food production chains in an expanding European market.
- To develop comparative safety assessment methods for foods produced by different breeding approaches and production practices, using modern profiling techniques, and new qualitative and quantitative risk assessment models.
- To investigate consumers' confidence and/or preferences in risk analysis practices for foods.

- To understand differences in food risk perceptions of consumers, experts, and decision-makers, and to design informative risk communication strategies that directly address societal concerns.
- To investigate the role of institutions across Europe involved in risk assessment and management given the greater interest of the consumer in taking a broader impact of food production on environment, animal welfare, sustainability, and socio-economic consequences into account.
- To design a new risk analysis approach for foods, integrating scientific principles, societal aspects, and effective public participation.

17.3.2 The SAFE FOODS Risk Analysis Framework

The integrated framework describes an iterative decision process consisting of four stages: framing, risk–benefit assessment, evaluation, and risk management (for a schematic overview, see Figure 17.3 [7–8]).

At the *framing* stage, interested parties, stakeholders, experts, and officials work together to gain an initial shared understanding of the issue, objectives, and broad

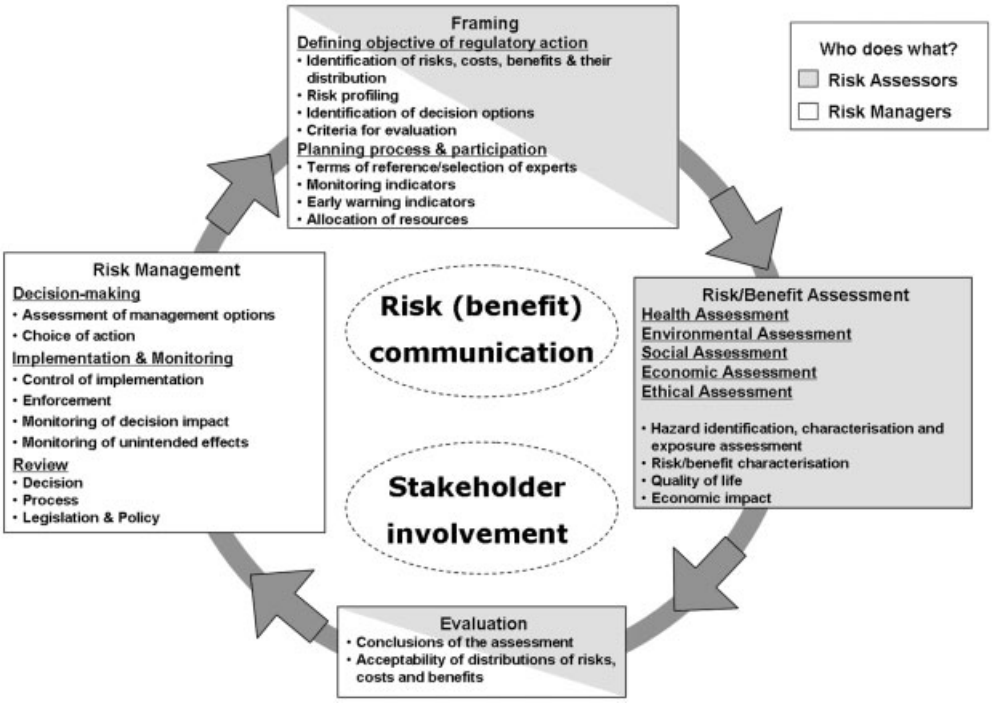

Figure 17.3 Risk analysis framework suggested by SAFE FOODS (adapted from [8]).

courses of regulatory action. Areas of consensus and dissent are documented in order to provide the basis for planning future decisions. Framing also includes defining the scope of the assessment, together with the terms of reference for those involved in the assessment process, proposing criteria for ranking regulatory options, together with monitoring indicators.

The *risk–benefit assessment* includes not only single pre-identified risks, but also human health impacts in general (including health benefits), as well as environmental, economic, social and ethical impacts, and their distribution. This reflects recent debate that has focused on extending the risk assessment paradigms applied in the process of risk analysis to include a broader assessment of the social, economic, and ethical impacts of hazards, whether this results from active risk prevention and mitigation or its omission. Social impact assessment, and its subcategory, health impact assessment, is a rapidly evolving area from the perspective of potential policy impact [9] and evolving assessment methodologies (see e.g. [10, 11]. However, inclusion of socio-economic and ethical impact aligns with the more general trend in policy to address the broader societal context in which risks are embedded.

The *evaluation* stage is proposed as an intermediate stage between risk assessment and management. Evaluation is a participatory process in which interested parties, stakeholders, experts, and officials use the assessment outcome to compare the risks, costs, and benefits and their distribution in the absence of any risk management measures. The outcomes of the evaluation are recommendations regarding which consequences are deemed acceptable, and whether risk management measures may be required.

In this context, *risk management* includes decision-making, implementation, monitoring, and review. Risk management involves the definition, ranking of alternative measures, and final selection of appropriate regulatory options in the context of the assessment outcomes and regulatory options available. Monitoring indicators are the result of proposals made at the framing stage. At the review stage, the impacts of the decision, together with the process by which the decision has been made, and the legislation under which the issue is regulated, are revisited and the effectiveness of what has been done assessed.

The three main differences from the other models described above (e.g., [1, 5], see sections 17.2.1. and 17.2.2, respectively) can be described as: (i) expansion of the scope of the formal risk assessment to include assessment of benefits and costs; (ii) more formal (and institutionalized) stakeholder participation; and (iii) improved risk communication and publicly accessible reports at each stage of the process.

17.3.3
Stakeholders' Views on the New Risk Analysis Framework

To assess the expert opinions on the new risk analysis framework, a Delphi survey [12] was used to solicit stakeholder and end-user views regarding the potential

utility of the new framework. Details of this survey are reported elsewhere [7]. The Delphi approach involves a degree of interactivity and dialog, similar to the kind of interactive dialog found in group meetings, but which enables access to wider expertise than might otherwise be attainable. In addition, the approach uses questionnaires to elicit the opinions, which provides a structured dialog. The methodology essentially involves the repeated surveying of experts, the opinions from whom are used as feedback on subsequent "rounds".

Within this Delphi study, the participants were first sent a questionnaire about the new framework, and then presented with a second survey containing similar questions, which they were asked to complete. In the second round, the experts were provided as well with anonymized feedback regarding the opinions of the whole group on the first round, either in the form of averaged results, or quotations derived from individual expert views, which may have resulted in them reconsidering their views. The views of two groups of experts in risk assessment, risk management, and risk communication were addressed, the first group with experts from within EU Member States, and the second with experts from outside of the EU.

The results suggested that most of the novel concepts in the model were acceptable to many of the experts, though those experts from within the EU seemed to be more positive than their counterparts from the international community. There was substantial support for the idea of broadening assessment to include socio-economic and ethical impacts. Furthermore, there was general support for increasing the role of other stakeholders in the overall risk analysis process. While there was broad stakeholder support for the use of these innovations, there was consensus that they should be applied on a case-by-case basis, rather than applied routinely, perhaps a decision to be made at the framing stage. Varying views existed, however, as to how stakeholders should be involved, what were the appropriate methodological approaches required to measure risks and benefits associated with the different impact factors, including health, and how these different factors should be weighted in the risk analysis process. Finally, the applicability of the new model to emerging risks, including those associated with new technologies, such as nanotechnology, required further discussion.

17.4
Risk Analysis and Nanotechnology

The case of nanotechnologies applied to food and agricultural production is presented here, as it provides an example of a new technology associated with potential new risks and benefits. The authors suggest that the integrated risk analysis framework discussed above can provide a balanced approach toward safe and prudent policies for development and integration of nanotechnology into the domain of food production and handling.

17.4.1 Background of Nanotechnology

Working at the atomic level only became within reach when key analytical tools such as the scanning tunneling microscope were developed in the 1980s. Advances like these and other analytical tools quickly spread to be utilized in many other fields of science. This has led to the development of materials showing unique properties that are dependent on their nanostructure, for example, nanoscale size. Current research is leading to the development of sophisticated and heterogeneous materials and devices, based on an increasing ability to engineer their functionality at the nanoscale [13]. In this context, it has been emphasized that the benefits that have the potential to change and improve our lives will inevitably bring with them new risks that need to be identified and managed [14], which of course emphasizes the need for the application of effective technology governance.

Nanotechnology itself and its applications are now rapidly growing, as hundreds of (claimed) nanotechnology products, including enhanced materials, electronic products and devices, and pharmaceutical products, are already on the market [15]. Nanotechnology applications are beginning to impact on the food-associated industries and are predicted to grow rapidly in the coming years. Applications in this area are already many and wide-ranging: the development of improved taste, color, flavor, texture, and consistency of foodstuffs; increased absorption and bioavailability of nutrients and health supplements; new food packaging materials with improved mechanical, barrier, and antimicrobial properties; and nanosensors for traceability and monitoring the condition of food during transport and storage [16–19].

It is this broadness of application of nanotechnologies that makes it particularly difficult to discuss potential risks in general terms. Moreover, this broadness also makes the technology very sensitive to any emerging consumer concerns about its application, because (negative) discussions about applications of nanotechnology in one sector are likely to have an effect on applications in another sector. This is also one of the reasons why the newly developed integrated SAFE FOODS risk analysis framework involving stakeholders in the framing and evaluation stages of the risk analysis process appears particularly suited for the topic of the safety of nanomaterials in food.

Nanotechnology is a collection of enabling and converging technologies, which mean that it is not a single type of technology used in a single field of science, but a great variety of techniques that have only one thing in common: the nanometer-size scale. Given that premise, it is useful to provide the definitions that have been applied to the field of nanotechnology and nanoparticles and which are used throughout this chapter:

> ***Nanotechnologies*** The design, characterization, production, and application of structures, devices, and systems by controlling shape and size at the nanometer scale [20].

Nanoparticle A discrete entity that has three dimensions of the order of 100 nm or less.

Nanoparticulate matter A substance comprising of particles, the substantial majority of which have three dimensions of the order of 100 nm or less [21].

Nanoparticles as such are not new to biology. Nano-sized particles can have a natural origin, such as sand dust, and ash resulting from volcanic eruption, or can be the unintended result of human activities, such as ultra-fine particles in diesel exhaust (combustion). In the remaining part of this chapter, the discussion will be solely dedicated to engineered nanoparticles:

Engineered nanoparticle Any material that is deliberately created such that it is composed of discrete functional parts, either internally or at the surface, many of which will have one or more dimensions of the order of 100 nm or less [21].

17.4.2 Historic Picture of Nanoparticle Safety in Relation to Risk Analysis and Good Governance

Recently, Oberdörster *et al.* [22] described the roots of nanotechnology from strands of knowledge gained during the development of modern particle toxicology (fine dust, pollution particles), virology, and other sciences.

It was not before 1990 that the size of (fine dust) particles was recognized as an important factor in its translocation over the lung epithelium. Before this period, possible contributions of fine or ultra-fine particles were not considered or imagined. But in the early 1990s, it was observed that a significantly greater pulmonary inflammation and interstitial translocation occurred from a given mass of ultra-fine particles than from the same mass of fine particles [23, 24]. The same scientists, two years later, concluded that "toxic responses to new technology metal compounds may not be extrapolated from known metal toxicology" [25]. Mechanistic research on effects caused by asbestos had also been initiated, which, in the mid-1990s, led to the "oxidative stress hypothesis" explaining the toxicity of ultra-fine particles including metal nanoparticles following inhalatory exposure [26–28].

It was in this same period that results from dose (metric) and pulmonary effect studies led to the conclusion that parameters such as particle surface area, size, and surface chemistry as key dose metric parameters explained the observed effects [29]. This list of parameters was subsequently extended by Oberdörster *et al.* [30] and Warheit *et al.* [31], who concluded that "knowledge about only one or two characteristics of nanoparticles is not sufficient to interpret their biological and toxicological effects".

In the last decade, an ever-increasing number of studies with engineered nanoparticles have been published. Both positive and negative aspects were highlighted, and these results, in turn, have been compiled in numerous reviews. It

was during this period that, for the first time, general concerns were raised about the unknown potential of some nanomaterials to pose a hazard to both human health and the environment. This also highlights the need for risk managers to be able to consider the benefits besides the risks of the new technology, of which the assessment is one of the new features recommended by the newly developed integrated SAFE FOODS risk analysis framework for food safety. The framework also provides for a mechanism of involving stakeholders during the framing stage of the risk analysis process, when issues to be addressed during the scientific stage of risk and benefit assessment are identified.

The challenges of nanotoxicology, that is, the branch of science focusing on the potential toxicity of nanomaterials, for science, industry, and regulators have been discussed in many conferences, workshops, and scientific committees. The need for toxicological testing of nanomaterials is clearly identified in the reports of these meetings [20, 32–35], which have also contributed to the growing awareness that an improved understanding of the hazards of nanomaterials is essential to enable a sustainable maturation of nanotechnologies. This is also reflected in the European Union's approach to the introduction of nanotechnology as being required to be "safe, integrated and responsible" [36]. In practical terms, the risk is likely to differ from one nanomaterial to another, ranging from safe and innocuous for most nanomaterials to highly toxic for some others [22].

17.4.2.1 **Risk Assessment**

Current safety and risk assessment requirements are based on knowledge gathered for conventional chemicals. In these assessments, knowledge gaps for less well-characterized chemicals may occasionally be encountered. Such uncertainties are approached on the basis of general knowledge, for example through extrapolation from a well-characterized compound to a similar, less well-characterized one. For nanoparticles, however, such a knowledge base is lacking, and, at the same time, the uncertainties in the safety assessments are also expected to be greater [37].

At this stage, the (lack of) knowledge about nanotoxicology may result in risk assessors basing their risk assessments on available, yet incomplete, information about nanoparticles and their appearance in products. Over time, it will be possible to obtain more comprehensive data and to extract the most relevant information for the risk assessment.

From a regulatory point of view, the question has been raised as to what information is additionally required for effective regulation of nanotechnology. In addition, the question has arisen as to whether the current regulatory system within the EU is suited to cope with the regulatory demands placed upon it in this context. To evaluate this, the EU has commissioned its Scientific Committees and Commission services, as well as EFSA in 2008, to perform a scientific and legislative review on the suitability of the existing regulation for nanotechnologies. The Scientific Committee on Emerging and Newly-Identified Health Risks (SCENIHR) concluded that the EU regulatory framework covers, in principle, also nanotechnologies [38]. In line with this, the Health Council of The Netherlands

considered that "the best course of action would be to modify existing laws and rules as and when developments within the fields of nanoscience and nanotechnologies render such measures necessary" [39]. SCENIHR and others deemed adjustments of legislation, guidelines, and guidance documents concerning the testing of nanoparticles of the substance to be necessary [38]. However, such adaptations can currently not be made due to the lack of knowledge on this topic.

It is clear that, in the existing regulatory framework, the responsibility for the safety of the product is assigned to the producers. There is currently a need for guidance on how to approach the safety assessment of nanoparticles, and to define what information should be presented by producers to the regulatory agencies. To further elaborate such guidance, a close collaboration among all stakeholders is required, for which the newly developed integrated SAFE FOODS risk analysis framework approach can serve as a useful model. In fact, such (early) stakeholder involvement is now being arranged at EU and national level, addressing not only the risks and benefits of the technology but also ethical issues. A typical example is the broad national debate initiated in 2008 in the Netherlands (http://www.nanopodium.nl/). In addition, large research programs are funded at EU and national level aimed to provide answers for the risk managers to improve the decision-making process.

17.5 Recommendations

Discussions on the improvement of the reliability of risk assessment of nanomaterials, data requirements, and expected performance of current assays have demonstrated that it is important to focus the question on what information is additionally required to dossier requirements for conventional chemicals. Some research agendas or roadmaps try to circumvent the uncertainties that are accepted in the risk assessment of conventional chemicals. In other words, in an area where such additional research questions can be or are being raised, it is essential to define those questions that represent the "need to know" issues. This approach should be leading all roadmaps or research agendas that are developed to be applicable to the field of potential risks of nanotechnology.

To improve the existing risk assessment methodology, good governance, and regulatory framework associated with the application of nanotechnology to food and agriculture, the following issues should be addressed in line with the proposed integrated SAFE FOODS risk analysis framework described above.

- Developing analytical tools for the detection and characterization of nanoparticles in food matrices to estimate exposure, kinetics, and toxicological dose–response relationships.
- Establishing dose metrics to facilitate the interpretation of scientific studies as well as regulatory frameworks.

- Investigating kinetics (especially oral bioavailability) and (oral) toxicity of the different types of nanoparticles, with special attention to those parts of the body that are normally protected by barriers like the blood–brain barrier and placenta.
- Assess the validity of currently used toxicological assays for detecting the effects caused by nanoparticles.
- Identifying products containing nanoparticles that are currently on the market (or being developed), including the type of nanoparticles that are (or will be) used and the estimated consumption of these products.
- Investigating the potential health benefits linked to the introduction of nanomaterials (e.g., packaging with antibacterial properties or nanosensors, higher bioavailability), as well as the economic, social, ethical, and environmental impacts of the application of the various forms of nanotechnology to food production and handling.
- Involving representatives of the relevant stakeholders' parties involved with the application of nanotechnology in food (e.g., consumers, producers) as well as the risk assessors and risk managers at the framing stage so as to ascertain that all relevant aspects and viewpoints are covered in the assessments of risks and benefits. Furthermore, these stakeholders should also be involved in the evaluation of the outcomes of the assessments in order to incorporate stakeholder views and priorities into decision options.

The request for extra information is not to be considered solely as a request for additional studies using new methodologies. It can also imply that conventional approaches and methodologies need to be redesigned. The use of novel technologies (e.g., profiling approaches) and the more frequent use of *in vitro* approaches for risk assessment need to be studied and used in parallel with conventional techniques.

In conclusion, the issue of governance of nanotechnology applied to food production represents an example of technological innovation requiring broader and more inclusive governance structures to be developed and applied, in order to meet the requirements and preferences of all key stakeholders, including the general public.

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