Food and Agriculture Organization of the United Nations

World Health Organization

FAO/WHO Expert Meeting on the Application of Nanotechnologies in the Food and Agriculture Sectors: Potential Food Safety Implications

MEETING REPORT

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iii. Declaration of interests

The Secretariat informed the expert meeting that all experts participating in the meeting had completed declaration of interest forms. Twelve experts among 17 declared an interest in the topics[1]. They were acknowledged by the participants, and were not considered as a potential conflict of interest in the meeting.

[1] The Secretariat had noted that the following two experts declaired an interest profiting from the private-sector activities. Dr Hans Biesalski declared that he conducted research, funded by a private company, in order to study the bioavailability of certain nano-carriers. Dr Jo Anne Shatkin declared that she provided consultancy work to private organizations.

iv. Abbreviations and acronyms

ADI	acceptable daily intake
ADME	absorption, distribution, metabolism, excretion
AFGC	Australian Food and Grocery Council
AUC	area under the curve
BBB	blood–brain barrier
bw	body weight
CGT	cyclodextrin glycosyl transferase
CIAA	Confédération des industries agro-alimentaires de l'UE (Confederation of the Food and Drink Industries of the EU)
CNT	carbon nanotube
CT	Cultura Theory
DLS	dynamic light scattering
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
EDS	energy dispersive system
EHS	environmental and health safety
EMEA	European Medicines Agency
ENM	engineered nanomaterial
EFSA	European Food Safety Authority
ESEM	environmental scanning electron microscope
EU	European Union
EVA	ethylene-vinylacetate
FAO	Food and Agriculture Organization of the United Nations
FCM	food contact material
FDA	US Food and Drug Administration
FEG-ESEM	field emission gun–environmental scanning electron microscope
FoE	Friends of the Earth
FSANZ	Food Standards Australia New Zealand
GI	gastrointestinal
GRAS	generally regarded as safe
IOMC	Inter-Organization Program for the Sound Management of Chemicals
ISO	International Organization for Standardization
JECFA	Joint FAO/WHO Expert Committee on Food Additives
MRL	Maximum residue limit
MWCNT	multi-wall carbon nanotube
N&N	nanoscience and nanotechnology
NGO	non-governmental organization
NISEnet	Nanoscale Informal Science Education Network
NOEL	no-observed-effect level
OECD	Organisation for Economic Co-operation and Development
OIE	World Organisation for Animal Health
PA	polyamide
PE	polyethylene
PEEK	polyether ether ketone
PEG	polyethylene glycol
PEI	polyether imides
PET	polyethyleneterephthalate
PLA	polylactic acid
PPS	polyphenylene sulphide
PS	polystyrene
PVC	polyvinylchloride
QD	quantum dots
QSAR	quantitative structure-activity relationship
RA	risk assessment

RFID	radio frequency identification display
RMF	risk management framework
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SEM	scanning electron microscope
SMC	Science Media Centre
SWCNT	single-wall carbon nanotube
TEM	transmission electron microscope
USDA/CSREES	United States Department of Agriculture/Cooperative State Research, Education, and Extension Service
UV	ultraviolet
UV-Vis	ultraviolet–visible spectroscopy
WHO	World Health Organization
XRD	X-ray diffractometry

v. Working definitions

The specific properties of nanomaterials derive from their nanoscale size, shape and potentially reactive surfaces, etc. There are a number of definitions that are aimed at capturing these materials and their properties, the nanofeatures, such as those proposed by the ISO, the SCENIHR and published more recently in the EFSA opinion (EFSA, 2009). The definitions given in Table 1 have been adopted for the FAO/WHO Experts meeting on nanotechnology applications for food and agriculture.

Table 1. Definitions for nanotechnologies adopted for the purposes of the FAO/WHO Expert Meeting on Nanotechnology Applications for Food and Agriculture
(Adapted from the opinions of ISO, 2008; SCENIHR, 2007b; EFSA, 2009.)

Term	Definition
Agglomerate	Collection of weakly bound particles or aggregates or mixtures of the two where the resulting external surface area is similar to the sum of the surface areas of the individual components. A group of particles (also termed secondary particles) held together by weak forces such as van der Waals forces, some electrostatic forces and/or surface tension.
Aggregate	Particle comprising strongly bonded or fused particles where the resulting external surface area may be significantly smaller than the sum of calculated surface areas of the individual components. A group of particles (also termed secondary particles) held together by strong forces such as those associated with covalent bonds, or those resulting from sintering or complex physical entanglement.
Aspect ratio	A ratio describing the primary dimension over the secondary dimension(s).
Coalescence	The formation of a new homogeneous entity out of two initial entities, e.g. after the collision of two nanoparticles or nanostructures.
Degradation	A breakdown in the physicochemical structure and/or organoleptic characteristics of a material.
Engineered nanomaterial (also known as manufactured nanomaterials)	Any material that is intentionally produced in the nanoscale to have specific properties or a specific composition.
Nanocarrier (or nanocapsule)	A nanoscale structure whose purpose is to carry and deliver other substance(s).
Nanocomposite	A multi-phase material in which the majority of the dispersed phase components are nanomaterials(s).
Nanocrystalline material	A material that is comprised of many crystals, the majority of which are in the nanoscale.
Nanomaterial	Any form of a material that has one or more dimensions in the nanoscale.
Nanoparticle	A discrete entity that has all three dimensions in the nanoscale.

Nanorod (nanofibre, nanowire, nanowhisker)	Materials shaped into rods, fibres, wires, whiskers, etc that have at least two dimensions in the nanoscale.
Nanoscale	Size dimensions typically between approximately 1 and 100 nm. This is the size range where material properties are more likely to change from bulk equivalents. The actual size range will depend on the functional properties under consideration.
Nanosheet	Nano-object with one external dimension in the nanoscale.
Nanostructure	Any structure that is composed of discrete functional parts, either internally or at the surface, of which one or more are in the nanoscale. Often used in a similar manner to 'nanomaterial'.
Nanotube	A discrete hollow fibre entity, which has two dimensions in the nanoscale.
Biopersistent	A substance that has been absorbed but is not readily broken down or excreted.

vi. Executive summary

Background

1. Governments, industry and science have identified the potential of nanotechnology in the food and agriculture sectors and are investing significantly in its application to food production. However, owing to limited knowledge of the effects of these applications on human health, the need for early consideration of the food safety implications of the technology is recognized by stakeholders.
2. In response to this accelerating development, FAO and WHO convened an Expert Meeting on the "application of nanotechnologies in the food and agriculture sectors: potential food safety implications" in order to identify further work that may be required to address the issue at global level.
3. Seventeen experts from relevant disciplines, such as food technology, toxicology and communication, met at FAO headquarters on 1–5 June 2009 and focused in working groups and during plenary sessions on three main areas: the use of nanotechnology in food production and processing; the potential human health risks associated with this use; the elements of transparent and constructive dialogues on nanotechnology among stakeholders.

Use of nanotechnology

4. Nanotechnology offers considerable opportunities for the development of innovative products and applications for agriculture, water treatment, food production, processing, preservation and packaging, and its use may bring potential benefits to farmers, food industry and consumers alike.
5. Nanotechnology-based food and health food products, and food packaging materials, are available to consumers in some countries already and additional products and applications are currently in the research and development stage, and some may reach the market soon. In view of such progress, it is expected that nanotechnology-derived food products will be increasingly available to consumers worldwide in the coming years.
6. Materials that are produced intentionally with structural features at a nanoscale range (between 1 and 100 nm) may have different properties when compared with their conventional counterparts. They will be employed in a variety of applications e.g. in food packaging materials where they will prevent microbial spoilage of food, as food additives modifying for example a food's texture and taste, in nutrients (e.g. vitamins) leading to increased bioavailability, and in agrochemicals where, for example, they will provide novel routes to deliver pesticides to plants. The impact on human health will depend on whether and how the consumer is exposed to such materials eventually, and whether these materials will behave differently compared to their conventional, larger dimensioned, counterparts .
7. The Expert Meeting recognized the need to agree on clear and internationally harmonized definitions related to the application of nanotechnologies to the food chain, and to develop a procedure for classifying nanostructures that would assist risk managers. At the international level, possible gaps in the food standard setting procedures as applied by the Codex Alimentarius Commission need to be identified and addressed.

Assessment of human health risks

8. The Expert Meeting acknowledged that the current risk assessment approaches used by FAO/WHO and Codex are suitable for engineered nanomaterials used in food and agriculture and emphasized that additional safety concerns may arise owing to the characteristic properties of nanomaterials, which need to be addressed.
9. As the size of the particles decreases, the specific surface area increases in a manner that is inversely, and non linearly proportional to size, until the properties of the surface molecules dominate. This results in novel features that are determined by the high surface-to-volume ratio, which may also give rise to altered toxicity profiles. This very high surface area of

engineered nanomaterials has consequences that need to be considered in their risk assessment, because it makes them different from their micro/macroscale counterparts.

10. As a result of their specific physicochemical properties, it is to be expected that nanoparticles may interact with other substances present in foods, such as proteins, lipids, carbohydrates and nucleic acids. Therefore, it is important that the effects and interactions of engineered nanomaterials are characterized in the relevant food matrix.
11. It is also important to consider life cycle aspects in the risk assessment of engineered nanomaterials, for example to analyse their fate in the environment, which may result in indirect human exposure to substances not used intentionally on food products.
12. The experts agreed that FAO/WHO should continue to review its risk assessment strategies, in particular through the use of tiered approaches, in order to address the specific emerging issues associated with the application of nanotechnologies in the food chain. A tiered approach might enable the prioritization of types or classes of materials for which additional data are likely to be necessary to reduce uncertainties in the risk assessment.
13. The experts recommended that FAO/WHO should encourage the innovative and interdisciplinary research that may lead to novel risk assessment strategies for the application of nanotechnologies in food (inclusive of water) and feed, while maintaining or improving the current level of protection. It was also agreed that the development of validated testing methods and guidance would help to address specific data gaps.

Stakeholder confidence and dialogue

14. The Expert Meeting analysed the general requirements for the engagement of stakeholders, which is acknowledged as imperative for any emerging or controversial issue in the area of food safety. The introduction of nanotechnology into foods and the ongoing corresponding discussion were considered with respect to the main interest groups that have been engaged so far, as were the initiatives for dialogues that have been started by governments, think tanks and international organizations.
15. It is understood that it will be critical to the success of a research strategy for nanomaterials to address the key interests, priorities, and concerns of stakeholders and ensure that pathways and potential risks are addressed by sponsored research.
16. The experts recognized that consumer attitudes towards the application of nanotechnology in food and agriculture are complex: they want to understand the potential risks and benefits of nanotechnology and they want clear tangible benefits. Without obvious benefits, consumers are unlikely to have positive impressions of nanotechnology-enhanced food products.
17. As a common denominator across nearly all advocacy groups, the experts identified the request for a discussion to determine the necessity of policy interventions on the introduction of nano-engineered particles and processes into commercial products for as long as the potential safety threats cannot be measured and evaluated adequately. Nearly all have expressed a desire for industry and governments to implement measures to protect the health and safety of workers and the public from the consequences of the unregulated release of commercial nanoproducts into the environment.
18. Greater access of scientists to the public debate, where their evidence and expert arguments can be shared, would support informed public debate and assist the public in forming their own conclusions once they have heard a rich mix of competent voices.
19. The meeting proposed that FAO/WHO should provide a forum for continued international dialogue to develop strategies to address stakeholder issues surrounding the development of nanotechnologies in food and agriculture.
20. FAO/WHO should encourage Member Countries to engage the public on applications of nanoscience and the nanotechnologies in food and agriculture. In support of this engagement, FAO/WHO should provide guidance, training, and capacity building resources for governments to engage stakeholders. FAO/WHO should also review the existing FAO/WHO food safety risk analysis framework in light of other analytical deliberative frameworks, in particular with regard to engaging stakeholders.

21. In recognition of its importance for the building of trust, the experts proposed that FAO/WHO identify mechanisms to support the need for transparency and traceability of nano-enabled products or engineered nanomaterials in food and agriculture and their associated risks. The importance of communication and cooperation with other inter-governmental organizations was stressed.

1 Introduction

1.1 Background

The advent of nanotechnology has unleashed enormous prospects for the development of new products and applications for a wide range of industrial and consumer sectors. The new technological developments have already opened up a multibillion dollar industry in recent years, the global market impact of which is expected to reach US$1 trillion by 2015, with around 2 million workers (Roco and Bainbridge, 2001). While the majority of manufacturing and use of nanoscale materials occurs in the United States, the European Union, with its around 30 percent global share of the sector, is not lagging far behind in this field (Aitken *et al.*, 2006; Chaudhry *et al.*, 2005). Like other sectors, nanotechnology promises to revolutionize the whole food chain – from production to processing, storage, and development of innovative materials, products and applications. Although the potential applications of nanotechnoloy are wide ranging, the current applications in the food and agricultural sectors are relatively few, because the science is still newly emergent. An overview of more than 800 nanotechnology-based consumer products that are currently available worldwide (Woodrow Wilson International Centre for Scholars, 2009), suggests that only around 10 percent of these are foods, beverages and food packaging products. However, nanotechnology-derived products and applications in these sectors have been steadily increasing in recent years, and are predicted to grow rapidly in the future. This is because the new technologies have a great potential to address many of the industry's current needs.

1.2 Market drivers and scale of commercial activity

Like any other sector, the food industry is driven by innovations, competitiveness and profitability. The industry is, therefore, always seeking new technologies to offer products with improved tastes, flavours, textures, longer shelf-life, and better safety and traceability. Other pressures, such as increased health consciousness amongst consumers and tighter regulatory controls, have also driven the industry to look for new ways to reduce the amount of salt, sugar, fat, artificial colours and preservatives in their products, and to address certain food-related ailments, such as obesity, high blood pressure, diabetes, cardiovascular diseases, digestive disorders, certain types of cancer (e.g. bowel cancer) and food allergies. The needs for food packaging have also changed with time, to stronger but lightweight, recyclable and functional packaging materials. "Smart" labels have been developed that can monitor food quality, safety and security during transportation and storage. Other "newer" societal and technological pressures are further shaping the food industry, such as the need to control pathogens and certain toxins in food, to reduce the amount of packaging and food waste, and to minimize the carbon footprint in the life cycle of food products and processes. In this context, the advent of nanotechnology has raised hopes that it can address many of these needs of the industry.

The main advantages that nanotechnologies offer over other existing technologies arise from the improved or novel functionalities of nanosized materials and substances (collectively termed nanomaterials), which also have a much larger surface to mass ratio compared with bulk equivalents. The very small size of nanomaterials enables dispersion of water-insoluble additives (such as colours, flavours and preservatives) in food products without the need for additional fat or surfactants. Nanosizing of bioactive substances is also claimed to give greater uptake, absorption and bioavailability in the body compared with bulk equivalents. Nanosized and nano-encapsulated ingredients and additives are used for the development of improved or new tastes, flavours and textures, and products with enhanced nutritional value. The advent of nanotechnologies has also enabled the development of innovative packaging materials, nanosensors and intervention technologies that can improve the safety, traceability and shelf life of food products. Such prospects have opened up a new wave of opportunities for a number of innovative developments in the agriculture, food and related sectors.

It is evident from the available reports that the sector applying nanotechnologies to food is led by the United States, followed by Japan and China (Helmut Kaiser Consultancy, 2004). There is a large potential for growth of the sector in developing countries. Despite the infancy of this nanofood sector, the overall size of the global market for nano-enabled products in 2006 has been estimated at around US$7 billion in 2006, and is predicted to grow to over US$20 billion by 2015 (Helmut Kaiser Consultancy, 2004). Another report, by the consulting firm Cientifica, has estimated the then current (2006) food applications of nanotechnologies at around $410 million (food processing US$100 million, food ingredients US$100 million and food packaging US$210 million). According to the report, the existing applications are mainly for improved food packaging, with some applications for delivery systems for nutraceuticals. The report estimated that by 2012 the overall market value would reach US$5.8 billion (food processing US$1303 million, food ingredients US$1475 million, food safety US$97 million and food packaging US$2.93 billion) (Cientifica, 2006). While nanotechnology-derived (health) food applications are growing worldwide, virtually all such applications are currently outside Europe, although some supplements and food packaging materials are available in the European Union (EU). However, considering the rapid developments in this field, and the global setup of major food companies, it is not unreasonable to anticipate that nanofood products will be increasingly available on the markets worldwide in the coming years.

It has been suggested that the number of companies currently applying nanotechnologies to food could be as high as 400 (Cientifica, 2006). It is believed that a number of major food and beverage companies have an active interest in application of nanotechnology in the areas relevant to the scope of this report.

1.3 Meeting background

Many countries have identified the potential of nanotechnology in the food and agriculture sectors and are investing significantly in its applications to food production. However, owing to our limited knowledge of the human health effects of these applications, many countries recognize the need for early consideration of the food safety implications of the technology.

In response to such requests, FAO and WHO considered that it was appropriate to convene an Expert Meeting on the "application of nanotechnologies in the food and agriculture sectors: potential food safety implications" in order to identify further work that may be required to address the issue at a global level.

As the first step, a Core Group was established to assist in organizing and planning the Expert Meeting. The Core Group provided recommendations on the best approach to elaborate advice on nanotechnology, and specifically addressed the scope and objectives of the Meeting, including the key issues to be discussed, the expertise required, and the need for review papers addressing key issues regarding the food safety implications of nanotechnology. The summary of the Core Group meeting's outcome note is attached in Appendix 1.

The Core Group noted that a food-chain approach was appropriate when considering the use of nanomaterials in primary production and their possible transmission to food products. In addition, nanomaterials may be recycled and could re-enter the food chain in this way.

In conclusion, the Core Group agreed the following three themes to be considered in the Expert Meeting:

- Existing and expected nanotechnology applications in the food and agriculture sectors;
- Assessment of human health risks associated with the use of nanotechnologies and nanomaterials in the food and agriculture sectors;
- Development of transparent and constructive dialogues among stakeholders.

FAO/WHO expert meetings are intended to provide guidance and advice to national governments on specific food safety related issues. Following the rules and procedures of joint FAO/WHO expert meetings, the call for experts and information (Appendix 2) was announced and 17 experts were selected by the selection committee according to the criteria described in the call for experts. Various key information materials were received as a response to the call for information, which were made available to the experts before the meeting; where considered relevant for the deliberations they have been included in the list of references.

In order to take stock of actual and anticipated activities involving nanotechnologies in the food and agriculture sectors, it was suggested that the Expert Meeting should involve representatives from key international agencies as resource persons to provide a briefing on their roles and the planned projects/activities/programmes linked to applications of nanotechnologies. Thus, resource persons from OECD, OIE and Codex Alimentarius were invited in addition to FAO/WHO sectoral (plant protection, animal health, nutrition and water quality) resource persons. The terms of reference for the resource persons are included in the briefing note for participants attached in Appendix 3.

1.4 Scope and objectives

Scope

The scope of the Expert Meeting covered actual and anticipated nanotechnologies applied in the food and agriculture sectors, with particular attention to:

- the application of nanotechnologies in all aspects of the primary production of foods of plant and animal origin;
- the application of nanotechnologies in food processing, packaging and distribution;
- the use of nanodiagnostic tools for detection and monitoring in food and agricultural production.
- Nanotechnologies applied in the environment were also included if there was a potential direct impact on food safety through the environment to the food chain.

The Expert Meeting was asked not to cover occupational health matters surrounding the use and application of nanotechnologies in the food and agriculture sectors, although these issues were noted for further consideration elsewhere.

Objectives

The overall purpose of the Expert Meeting was to provide member countries with comprehensive information on what was currently known about potential food safety risks, to identify priority areas of work required to better assess these risks, and to advise on ways to promote transparent and constructive dialogue among stakeholders.

To this end, the objectives of the Expert Meeting were the following:

- to take stock of actual and anticipated applications of nanotechnologies in the food and agriculture sectors;
- to identify potential food safety implications associated with actual and anticipated applications of nanotechnologies in the food and agriculture sectors;
- to determine the need for additional tools or metrics and to identify any data requirements and research gaps;
- to consider the application of current risk assessment methodologies to evaluate the safety of nanomaterials used in the food chain;
- to identify priority areas for which scientific advice should be requested from FAO/WHO in accordance with their Joint framework for the provision of scientific advice; and
- to advise on ways and means of fostering transparent and trustful dialogue among all stakeholders.

1.5 Expected outputs

The Expert Meeting was intended to:

- provide information on existing and emerging applications of nanotechnologies, including what was known about the food safety implications as well as any potential risks and the current capacity to assess such risk;
- formulate (or recommend) a medium-term plan of further work that may be required to assess those risks accurately;
- provide an analysis of efforts that have been made in various countries to promote communication among stakeholders and to advise on ways to facilitate transparent and constructive dialogue.

2 Existing and projected applications of nanotechnology in the food and agriculture sectors

2.1 Scope and objectives

While nanotechnologies offer many opportunities for innovation, the use of nanomaterials in food and agricultural applications has also raised a number of safety, environmental, ethical, policy and regulatory issues. The main issues relate to the potential effects and impacts on human health and the environment that might arise from exposure to nanosized materials.

This chapter presents an overview of the wide range of current and projected applications of nanotechnologies in the food and agriculture sectors. Other applications that may lead to human exposure to nanoparticles through the environment to the food chain have also been considered. The chapter provides information on the known and projected applications of nanotechnology, the scope and purpose of the applications, the types and forms of nanomaterials used, the availability of relevant products on market, and the potential for human exposure to nanoparticles. The chapter thus summarizes the state of the art with regard to applications of nanotechnology in agriculture and food production, and for food ingredients, additives, supplements and materials that contact food.

The information presented in this chapter has been collated from a variety of sources that include published literature, company websites, patent databases, national and international inventories, market analysis reports, key scientific reviews and reports, material presented at conferences, workshops and symposia, and through contacts with leading experts in the areas of nanotechnology applications (Chaudhry *et al.*, 2007; 2008).

It is also worth mentioning that some of the currently available information (especially through the Internet) is aimed largely at projecting the "magic" of nanotechnologies when applied to the food and agricultural sectors, and as such does not provide any concrete evidence that can be related to a "real" product or application that is either available now or can be expected in a few years' time. This chapter has, therefore, scrutinized the available information objectively, and discusses only the products and applications that are identifiable as existing, or in the research and development (R&D) pipeline, rather than those that are merely speculative[2].

2.2 Introduction

It was suggested some time ago that the properties of materials may be manipulated at very small scales (Feynman, 1959). The advent of nanotechnology has provided a systematic way to study and manipulate material properties on the nanoscale with a regularity and precision hitherto unknown. In this regard, the main focus has been on nanomaterials that are manufactured specifically to achieve a certain property or composition. In many products and applications, such as plastic materials for food packaging, nanomaterials may be incorporated in a fixed, bound or embedded form, and hence may not pose any new or additional risk to consumer health or the environment (if used and disposed of properly). Other applications may pose a greater risk of exposure for consumers to free engineered nanomaterials (ENMs), for example certain foods and beverages that may contain free nanoparticles, or a nanopesticide formulation that may be released deliberately into the environment.

A cursory overview of the current and projected applications of nanotechnologies suggests that many of them have emerged from similar technologies developed in related sectors, in particular pharmaceutical, medical and cosmetic sectors. The cross-cutting nature of nanotechnologies means that materials and applications developed in one sector are gradually finding their way into other related sectors (Cientifica, 2006; Chaudhry *et al.*, 2008). This is also because there is a certain degree of overlap between the food, medicine and cosmetic sectors. Many food products are marketed as a means to enhance nutrition, and as an aid to health, beauty and well-being. These subsectors, e.g.

[2] "It may be promising one day to make food from component atoms and molecules, the so-called 'Molecular Food Manufacturing" (Cientifica, 2006).

health foods, supplements, nutraceuticals, cosmeceuticals and nutricosmetics, appear to be the first target of nanotechnology applications. Thus, a large majority of the currently available nanotechnology-derived products falls into the categories of supplements, health foods and nutraceuticals, with currently only a few products in the food and beverage categories.

A number of recent reports and reviews have identified the current and short-term projected applications of nanotechnologies for the food sector (Bouwmeester *et al*., 2007; Chaudhry *et al*., 2008; Food Safety Authority of Ireland, 2008; Groves, 2008; Kuzma & VerHage, 2006; Morris, 2008). The main areas of application include food packaging and food products that contain nanosized or nano-encapsulated ingredients and additives. The main principle behind the development of nanosized ingredients and additives appears to be directed towards enhanced uptake and bioavailability of nanosized substances in the body, although other benefits, such as improvement in taste, consistency, stability and texture, etc., have also been claimed (Chaudhry *et al*., 2008).

The major area of application for ENMs is in materials that contact food, such as innovative packaging concepts aimed at developing innovative ENM–polymer composites that have improved mechanical properties or antimicrobial activity, and nano(bio)sensors for innovative labelling of packaged food products. The applications of ENMs in food packaging have been estimated to account for the largest share of the current and short-term predicted market for nanofood applications (Cientifica, 2006).

The other current and short-term projected applications of nanotechnologies include nanosized or nano-encapsulated ingredients and additives for a variety of applications in the food and agricultural sectors. These have been summarized in Appendix 4. A recent review by Chaudhry *et al.* (2008) has identified the following main categories of known and projected applications for the food and health food areas:

- where food ingredients have been processed or formulated to form nanostructures;
- where nanosized or nano-encapsulated additives have been used in food;
- where ENMs have been incorporated into coatings and packaging materials to develop innovative food contact surfaces and materials, and nano(bio)sensors for "Smart" packaging;
- where nanomaterials have been used in nanofiltration for the removal of undesirable components from foodstuffs;
- where applications of ENMs have been suggested for pesticides, veterinary medicines and other agrochemicals for improved food production systems.

2.3 Processed nanostructures in food

A key area of application of nanotechnology in food processing involves the development of nanostructures (also termed nanotextures) in foodstuffs. The mechanisms commonly used for producing nanostructured food products include nano-emulsions, surfactant micelles, emulsion bilayers, double or multiple emulsions and reverse micelles (Weiss *et al*., 2006). Examples of nanotextured foodstuffs include spreads, mayonnaise, cream, yoghurts, ice creams, etc. The nanotexturing of foodstuffs has been claimed to give new tastes, improved textures, consistency and stability of emulsions, compared with equivalent conventionally processed products. A typical benefit of this technology could be in the form of a low-fat nanotextured food product that is as "creamy" as the full-fat alternative, and hence offers a "healthy" option to the consumer. Currently, there is no clear example of a proclaimed nanostructured food product that is available commercially, although some products are believed to be at the R&D stage, and some may be nearing the market. One such example is a mayonnaise, which is an oil in water emulsion that contains nanodroplets of water inside the oil droplets. The mayonnaise may offer taste and texture attributes similar to the full-fat equivalent, but with a substantial reduction in fat intake by the consumer.[3]

[3] www.leatherheadfood.com

Another area of application involves the use of nanosized or nano-encapsulated food additives. This type of application is expected to exploit a much larger segment of the health food sector, and encompasses colours, preservatives, flavourings and supplements. The main advantages claimed include better dispersion of water-insoluble additives in foodstuffs without the use of additional fat or surfactants, and enhanced tastes and flavours owing to the enlarged surface area of nanosized additives, compared with conventional forms. A number of consumer products containing nanosized additives are already available in some food sectors, including foods, health foods, supplements and nutraceuticals. These include minerals, antimicrobials, vitamins, antioxidants, etc. Virtually all of these products are claimed to have improved absorption and bioavailability in the body compared with their conventional equivalents.

Another example is the increasing trend towards nanomilling of functional herbs and other plants, such as in the manufacture of green tea and ginseng.

2.4 Nanodelivery systems based on encapsulation technology

Nano-encapsulation in the form of micelles, liposomes or biopolymer-based carrier systems has been used to develop delivery systems for additives and supplements for use in food and beverage products. Nano-encapsulation is the technological extension of microencapsulation, which has been used by the industry for food ingredients and additives for many years. Nano-encapsulation offers benefits that are similar to, but better than, those of microencapsulation, in terms of preserving the ingredients and additives during processing and storage, masking unpleasant tastes and flavours, controlling the release of additives, better dispersion of water-insoluble food ingredients and additives, as well as improved uptake of the encapsulated nutrients and supplements. The modified optical characteristics of nanocarriers mean that they can be used in a wide range of products, such as clear beverages. The improved uptake and bioavailability alone has opened up a vast area of applications in food products that incorporate nanosized vitamins, nutraceuticals, antimicrobials, antioxidants, etc. After food packaging, nano-encapsulation is currently the largest area of nanotechnology application in the food sectors, and a growing number of products based on nanocarrier technology are already available on the market.

There is a variety of nanomicelle-based supplements and nutraceuticals that are available in some countries. Examples of these include a nanomicelle-based carrier system for the introduction of nutrients and supplements into food and beverage products. Other examples include nanostructured supplements based on self-assembled liquid structures. Acting as carriers for targeted compounds (e.g. nutraceuticals and drugs), these nanosized vehicles comprise expanded micelles in the size range of ~30 nm. An available example is a vegetable oil enriched in vitamins, minerals and phytochemicals. Other technology is based on a nanocluster delivery system for food products. A number of products are available based on this system. One example is a slimming product based on cocoa nanoclusters, which are coated on the surface of an ENM to enhance the chocolate flavour through the increase in surface area that hits the taste buds. Self-assembled nanotubes from the hydrolysed milk protein α-lactalbumin, which show good stability, have recently been developed (Graveland-Bikker and de Kruif, 2006). α-Lactalbumin is already used as a food ingredient, mainly in infant formulas. These food-protein derived nanotubes may provide a new carrier for nano-encapsulation of nutrients, supplements and pharmaceuticals.

The concept of nanodelivery systems seems to have originated from research on the targeted delivery of drugs and therapeutics. While it can offer many benefits to the consumer from increased absorption, uptake and improved bioavailability of nutrients and supplements, it also has the potential to alter the distribution of the substances in the body. For example, certain water-soluble compounds (e.g. vitamin C) have been rendered fat dispersible through nanocarrier technology, and vice versa: fat-dispersible compounds (e.g. vitamin A) have been rendered water dispersible. If the nanocarrier is broken down and its contents released into the gastrointestinal (GI) tract, the encapsulated compounds will not differ from their conventional equivalents. However, if a nanocarrier is capable of delivering the substance to the bloodstream, its ADME (absorption, distribution, metabolism, excretion)

characteristics may be different from the conventional forms. A significant change in bioavailability and/or tissue distribution of certain substances, compared with conventional bulk equivalents, may require a new risk assessment. These applications may also require investigations into the possible role of nanocarriers as a "Trojan Horse", in terms of facilitating the translocation of encapsulated substances or other foreign materials to unintended parts of the body.

2.5 Nanomaterials relevant to food applications

The currently available information suggests that nanomaterials used in food applications include both inorganic and organic substances. In addition to the engineered nanomaterials, there is a possibility that certain microscale materials used in food and feed applications may contain a nanoscale fraction owing to natural variation in size range (EFSA, 2009). Based on the available information, the ENMs likely to be found in nanofood products fall into three main categories: inorganic, surface functionalized materials, and organic ENMs (Chaudhry *et al.*, 2008). Examples of these include:

Inorganic nanomaterials
A number of inorganic ENMs are known to be used in food and health food products and food packaging applications. These include ENMs of transition metals such as silver and iron; alkaline earth metals such as calcium and magnesium; and non-metals such as selenium and silicates. Other ENMs that can potentially be used in food applications include titanium dioxide.

Food packaging is the major area of application of metal (oxide) ENMs. Example applications include plastic polymers with nanoclay as a gas barrier, nanosilver and nanozinc oxide for antimicrobial action, nanotitanium dioxide for ultraviolet (UV) protection, nanotitanium nitride for mechanical strength and as a processing aid, nanosilica for surface coating, etc.

Nanosilver: Nanosilver is finding a growing use in a number of consumer products, including food and health food, water, and food contact surfaces and packaging materials. Indeed, the use of nanosilver as an antimicrobial, antiodourant, and a (proclaimed) health supplement has already surpassed all other ENMs currently in use in different sectors (Woodrow Wilson International Centre for Scholars, 2009). Most current uses of nanosilver relate to health food and packaging applications, but its use as an additive to prepare antibacterial wheat flour is the subject of a recent patent application (Park, 2006).

Nanosilica: Amorphous nanosilica is known to be used in food contact surfaces and food packaging applications. Amorphous silica has been used for many years in food applications, such as in clearing of beers and wines, and as a free flowing agent in powdered soups. The conventional bulk form of silica is a permitted food additive (SiO_2 INS 551), but the material may not have been tested with a focus on nanosilica. Porous silica is used in nanofiltration to remove undesired components in food and beverages – such as the bitter taste in some plant extracts.

Nanotitanium dioxide: The conventional bulk form of titanium dioxide is already approved as an additive for food use (TiO_2 INS 171), but the conventional form may also contain a nanosized fraction. Nanotitanium dioxide is used in a number of consumer products (e.g. paints, coatings) and its use may extend to foodstuffs. For example, a patent (US Patent US5741505) describes the potential application of nanoscale inorganic coatings directly on food surfaces to provide a barrier to moisture and oxygen and thus improve shelf life and/or the flavour impact of foods. The materials used for the nanocoatings, intended to be applied in a continuous process as a thin amorphous film of 50 nm or less, include titanium dioxide (along with silicon dioxide and magnesium oxide). The main intended applications described in the patent include confectionary products. However, to our knowledge this technology has not been used in any commercial application. Nanotitanium dioxide is also known to be used as a photocatalyst in water treatment applications – especially to oxidize heavy metals and organic pollutants and to kill microbial pathogens.

Nanoselenium is being marketed as an additive to a green tea product, with a number of (proclaimed) health benefits resulting from enhanced uptake of selenium.

Nanocalcium salts are the subject of patent applications (Sustech GMBH & Co, 2003, 2004) for intended use in chewing gums. Nanocalcium and nanomagnesium salts are also available as health supplements.

Nano-iron is available as a health supplement. Nano-iron is also used in the treatment of contaminated water, where it is claimed to decontaminate water by breaking down organic pollutants and killing microbial pathogens.

An example of a soluble nanomaterial under development is **nano-salt**, which will enable consumers to cut down their salt intake because a small amount will cover a larger area of the food surface.

Surface functionalized nanomaterials

Surface functionalized nanomaterials are the second-generation ENMs that add certain types of functionality to the matrix, such as antimicrobial activity or a preservative action through absorption of oxygen. For food packaging materials, functionalized ENMs are used to bind with the polymer matrix to offer mechanical strength or a barrier against movement of gases, volatile components (such as flavours) or moisture. Compared to inert nanomaterials, they are more likely to react with different food components, or become bound to food matrices, and hence may not be available for migration from packaging materials, or translocation to other organs outside the GI tract. One example is the use of functionalized nano-clays in food packaging to develop materials with enhanced gas-barrier properties. The nanoclay mineral is mainly montmorillonite (also termed as bentonite), which is a natural clay obtained from volcanic ash/rocks. Nanoclay has a natural nano-scaled layer structure and is organically modified to bind to polymer matrices.

Organic nanomaterials

A number of organic nano-sized materials (many of them naturally-occurring substances) are used (or have been developed for use) in food/feed products. These include substances encapsulated in nanodelivery systems (section 8.4). Examples include vitamins, antioxidants, colours, flavours and preservatives. The main principle behind the development of nanosized organic substances is their increased uptake and absorption and improved bioavailability in the body, compared with conventional bulk equivalents. There is a wide range of materials available in this category, for example food additives (e.g. benzoic acid, citric acid, ascorbic acid) and supplements (e.g. vitamins A and E, isoflavones, β-carotene, lutein, omega-3 fatty acids, coenzyme-Q10). An example of an organic nanomaterial is the tomato carotenoid lycopene. A synthetic nanosized form of lycopene, a carotene occurring in tomatoes, has been produced. A water-dispersible product with a reported particle size in the range of 100 nm for use as a synthetic form of lycopene in food and beverages, in a water-dispersible form, is claimed to be available commercially. Lycopene was notified as of GRAS status (generally regarded as safe) to the FDA in the United States (GRAS Notice GRN000119/2002), and a recent EFSA opinion has considered its use in food and beverages as safe (EFSA, 2008). However, the evaluations by EFSA and JECFA did not include any nanoscale product form[4]. It is therefore not clear whether this material is currently used in any food or beverage product. A number of other nanosized food colours, preservatives and flavours are being developed and some may become available in the coming years.

It is worth mentioning that, in addition to the nanomaterials mentioned in this section, there are a number of other nanomaterials that are currently used for non-food applications but have not been considered here because they are not likely to be used for any application that is relevant to the scope of this paper. For example, certain carbon-based nanomaterials (fullerenes, carbon nanotubes) are

[4] It should also be noted that JECFA discussed at this meeting issues that food additives in nanoform would raise and concluded that "neither the specifications nor the ADIs for food additives that have been evaluated in other forms are intended to apply to nanoparticulate materials." (WHO, 2007).

used for different non-food applications, but are not likely to be used in food applications. This is because the functionalities that such materials offer mainly relate to enhanced mechanical strength and electrical conductivity, both of which are of little relevance to potential use in food products. However, there may be some applications of carbon nanotubes in the packaging area or water treatment. In addition to the nanomaterials added deliberately, foodstuffs may contain certain other nanomaterials, e.g through environmental contamination, migration from packaging, contact with active surfaces, or from the use of nanosized agrochemicals, pesticides or veterinary medicines.

2.6 Nano-enabled food contact materials (FCMs) and packaging

Nanotechnology applications for FCMs and food packaging constitute the largest share of the current and short-term predicted market for applications in the food sector (Chaudhry *et al*., 2008; Cientifica, 2006). While most applications of nanotechnology in the food and agriculture sectors are currently at R&D or near-market stages, the applications for food packaging are rapidly becoming a commercial reality. The contributing factors to these developments include significant benefits in terms of lightweight but strong packaging materials and prolonged shelf life of packaged foodstuffs, and the likely low risk to the consumer attributable to the fixed or embedded nature of ENMs in plastic polymers. A number of nanotechnology-derived FCMs are currently available worldwide, the main areas of application of which fall into the following broad categories:

- FCMs incorporating nanomaterials for improved packaging properties (flexibility, gas barrier properties, temperature/ moisture stability);
- "active" FCMs incorporating nanoparticles with antimicrobial or oxygen scavenging properties;
- "intelligent" and "Smart" food packaging, which incorporates nanosensors to monitor and report the condition of the food;
- biodegradable polymer–nanomaterial composites, with enhanced mechanical and functional properties.

Examples of the nanotechnology-derived FCMs that are either available, or are currently under R&D, are given below.

Nanoparticle reinforced materials
Also termed "nanocomposites", these are polymers reinforced with small quantities (up to 5 percent by weight) of nanosized particles, which have high aspect ratios and are able to improve the properties and performance of the polymer.

Polymer composites with nanoclay: These are among the first nanocomposites to emerge on the market as improved materials for packaging (including food packaging). Nanoclay has a natural nanoscaled layer structure, which when incorporated into polymer composite restricts the permeation of gases. Nanoclay–polymer composites have been made from a thermoset or thermoplastic polymer reinforced with nanoparticles of clay. These include polyamides (PA), nylons, polyolefins, polystyrene (PS), ethylene-vinylacetate (EVA) copolymer, epoxy resins, polyurethane, polyimides and polyethyleneterephthalate (PET). There are a number of nanoclay–polymer composites available commercially. Known applications of nanoclay in multilayer film packaging include bottles for beer, carbonated drinks and thermoformed containers[5]. Some large breweries are reported to be using the technology already in their beer bottles[6].

Polymer composites with nano-metals or metal oxides: Polymer nanocomposites incorporating metal or metal oxide nanoparticles are utilized mainly for their antimicrobial action, abrasion resistance, UV absorption, and strength. Some nanomaterials have been used to develop active packaging that can absorb oxygen and therefore keep food fresh. Other nanomaterials have been

[5] Plastic Technology www.plastictechnology.com/articles/200508fa1.html
[6] Big Idea Investor: www.bigideainvestor.com/index.cfm?D=603

incorporated as UV absorbers to prevent UV degradation in plastics such as PS, PE and PVC. The commercially important nanomaterials in this respect include nanosilver and nanozinc oxide for antimicrobial action, nanotitanium dioxide for UV protection in transparent plastics, nanotitanium nitride for mechanical strength and as a processing aid, and nanosilica for surface coating.

It is important to note that the surface biocides, such as nanosilver, in packaging materials are not intended to have a preservative effect on the food. Instead, the biocidal agent is intended to help maintain the hygienic condition of the surface by preventing or reducing microbial growth. Where the use of a nanomaterial gives a preservative effect in the packaged product, there would be a requirement for additional regulatory authorization as a direct food additive in most countries. Based on the antimicrobial action of nanosilver, a number of "active" FCMs have been developed that are claimed to preserve the food materials by inhibiting the growth of micro-organisms. Examples include food storage containers and plastic storage bags. Nanosilver has also been incorporated into the inner surface of some domestic refrigerators to prevent microbial growth and maintain a clean and hygienic environment in the fridge. The discovery of antimicrobial properties of nanozinc oxide and nanomagnesium oxide at the University of Leeds may provide more affordable materials for such applications in food packaging (Zhang *et al.*, 2007). A plastic wrap containing nanozinc oxide is also available, which is claimed to sterilize under indoor lighting.

Coatings containing nanoparticles: Coatings that contain nanoparticles are used to create antimicrobial, scratch resistant, anti-reflective, or corrosion-resistant surfaces. This involves the coating of nanoparticulate form of a metal, metal oxide or a film resin substance with nanoparticles. Examples of FCMs with nanocoating include antibacterial kitchenware, cutting boards and teapots.

High-barrier nanocoatings have also been developed that contain numerous nanodispersed platelets per micron of coating thickness to increase the barrier properties of PET; this enhances the oxygen barrier when used in food and drink applications, ensuring longer shelf life. The coatings have been reported to be very efficient at keeping out oxygen and retaining carbon dioxide and can rival traditional active packaging technologies such as oxygen scavengers (Garland, 2004). Examples include a nanocoating which is an aqueous-based nanocomposite barrier coating that provides an oxygen barrier with a 1–2 micron coating for food packaging use, and plasma arc deposition of amorphous carbon inside PET bottles as a gas barrier.

Antimicrobial nano-emulsions: Nano-emulsions have been developed for use in the decontamination of food packaging equipment and in the packaging of food. A typical example is a nanomicelle-based product which is claimed to contain natural glycerine and removes pesticide residues from fruits and vegetables, as well as the oil/dirt from cutlery.

Intelligent packaging concepts based on nanosensors

Nanotechnology has also enabled the development of nanosensors that can be applied as labels or coatings to add an intelligent function to food packaging in terms of ensuring the integrity of the package through detection of leaks (for foodstuffs packed under vacuum or inert atmosphere), indications of time–temperature variations (e.g. freeze–thaw–refreezing), or microbial safety (deterioration of foodstuffs).

Examples include an indicator that turns from transparent to blue, informing the consumer that air has entered the modified atmosphere of the packaged materials. For this type of application, nanotechnology-derived printable inks have been developed. One example is an oxygen detecting ink containing light-sensitive (TiO_2) nanoparticles, which only detect oxygen when they are "switched on" with UV light. Other conductive inks for ink jet printing based on copper nanoparticles have also been developed (Park *et al.*, 2007). Food safety also requires confirmation of the authenticity of products. This is where application of nanobarcodes incorporated into printing inks or coatings has shown the potential for use in tracing the authenticity of the packaged product (Han *et al.*, 2001).

Food quality indicators have also been developed that provide visual indication to the consumer when a packaged foodstuff starts to deteriorate. An example of such food quality indicators is a label based on detection of hydrogen sulphide, which is designed for use on fresh poultry products. The indicator is based on a reaction between hydrogen sulphide and a nanolayer of silver (Smolander *et al.*, 2004). The nanosilver layer is opaque light brown, but when meat starts to deteriorate silver sulphide is formed and the layer becomes transparent, indicating that the food may be unsafe to consume.

Other materials developed for potential food packaging applications are based on nanostructured silicon with nanopores. The potential applications include detection of pathogens in food and variations of temperature during food storage. Another relevant development is aimed at providing a basis for intelligent preservative packaging technology that will release a preservative only when a packaged food begins to spoil (ETC Group, 2004).

2.7 Use of nanotechnologies in the agriculture sector

The apparent benefits of substituting active ingredients or carriers with nanosized equivalents has also opened the door to research into potential applications of nanotechnology to pesticides, veterinary medicines and other agrochemicals such as fertilizers and plant growth regulators. The anticipated benefits, which are driving R&D in these areas, include a potential reduction in the use of certain agrochemicals (such as pesticides) and a better ability to control the application and dosage of active ingredients in the field. Despite a great deal of industrial interest in this area, examples of available products are very few and far between. Most developments seem to be currently at the R&D stage, and it is likely that the agriculture sector will see some large-scale applications of nanotechnologies in the future. Should this occur, this will increase the potential exposure to agrochemicals used in the agriculture sector (MacKenzie, 2007).

Animal feed

Theoretically, any nanosized mineral, vitamin or other additive/supplement developed for a food application can equally be used for animal feed, although the high cost of using food-grade additives for animal feed may be an obvious issue. There are a few examples of available products where a nanosized additive has been specifically developed (or is under development) for animal feed. An example is a feed additive comprising a natural biopolymer from yeast cell walls that can bind mycotoxins to protect animals against mycotoxicosis. Nano(feed)grade liquid vitamin mixes are also available for use in poultry and livestock feed. Other developments at the R&D stage include an aflatoxin-binding nano-additive for animal feed, which is derived from modified montmorillonite (nanoclay) (YingHua *et al.*, 2005). Researchers have developed a nanoparticle that adheres to *E. coli* consisting of a polystyrene (PS) base, polyethylene glycol (PEG) linker, and mannose targeting biomolecule. These nanoparticles are designed to be administered through feed to remove food-borne pathogens in the GI tracts of livestock, and their potential risks, benefits and societal issues have been explored (Kuzma *et al.*, 2008).

Agrochemicals

Research is also being carried out into the development of various nanosized agrochemicals, such as fertilizers, pesticides and veterinary medicines. The use of nanosized active ingredients has been suggested to offer improved delivery of agrochemicals in the field, better efficacy of pesticides and better control over dosing of veterinary products. For example, nano-encapsulated and solid lipid nanoparticles have been explored for the delivery of agrochemicals (Frederiksen *et al.*, 2003); these include slow- or controlled-release fertilizers and pesticides. One example is a combined fertilizer and pesticide formulation encapsulated in nanoclay for the slow release of growth stimulants and biocontrol agents, which has been tested under the Pakistan–US Science and Technology Cooperative Program 2006 (Friends of the Earth, 2008).

The development of a nano-emulsion (water/poly-oxyethylene) nonionic surfactant (methyl decanoate) containing the pesticide beta-cypermethrin has been described by Wang *et al.* (2007b).

Porous hollow silica nanoparticles, developed for the controlled delivery of the water-soluble pesticide validamycin with a high loading capacity (36 wt%), have been shown to have a multistaged release pattern (Liu *et al*., 2006). Similarly, the development of organic–inorganic nanohybrid material for controlled release of the herbicide 2,4-dichlorophenoxyacetate has been described by Bin Hussein *et al.* (2005). The study used zinc–aluminium layered double hydroxide to host the herbicide active ingredient by self-assembly. A few fertilizers claimed to contain nanosized micronutrients (mainly oxides and carbonates of zinc, calcium, magnesium, molybdenum, etc.) are available. A micronized (volcanic) rock dust is available from a variety of sources for remineralization of soil. A commercial product, which comprises sulphates of iron, cobalt, aluminium, magnesium, manganese, nickel and silver, is available for treatment of seed and bulbs before planting. The product claims to have been derived from nanotechnology but the particle size range is not given. Research and development into slow- or controlled-release fertilizers is being carried out in China and India.

The use of nanoforms of agrochemicals offers a number of potential benefits in terms of reduced use of chemicals, but may also raise concerns over exposure of agricultural workers, and contamination of agri-food products. Apart from the intentional use of nanotechnologies in agrifood sectors, there may be instances where ENMs can get into food and drinks through environmental contamination. A study by Boxall *et al.* (2007)[7] identified possible routes of exposure through environmental contamination from the manufacture, use and disposal of consumer products containing ENMs. The main products and materials identified include cosmetics and personal care products (TiO_2, ZnO, fullerene (C60), Fe_2O_3, Ag, Cu, Au), catalysts, lubricants and fuel additives (CeO_2, Pt, MoS_3), paints and coatings (TiO_2, SiO_2, Ag, quantum dots), water treatment and environmental remediation (Fe, Fe–Pd, polyurethane), agrochemicals (porous SiO_2 carriers and other nanosized agrochemicals), food packaging (Ag, nanoclay, TiO_2, ZnO, TiN), nanomedicine and carriers (silver, Fe, magnetic ENMs).

2.8 Future perspectives

Introduction

An understanding of the current R&D activities in the area of nanofood also provides an insight into the possible future developments. It has been estimated that over 200 companies worldwide are conducting R&D into the use of nanotechnology in engineering, processing, packaging or delivering food and nutritional supplements (Cientifica, 2006; IFST, 2006). While only a handful of food and health food products containing nano-additives are currently available, it has been estimated that over 150 applications of nanotechnology in food may be at different stages of development (Cientifica, 2006). A search of patent databases found more than 460 patent entries relevant to applications of nanotechnology in food or food contact materials (Chaudhry *et al.*, 2007). The main relevant R&D themes are aimed at:

- reducing the amount of salt, fat, colour, or other additives to promote healthy option foods;
- improving the appearance of food, e.g. by altering the colour, flavour, texture, consistency, and developing new tastes and sensations in the mouth;
- controlling the release of flavours and nutrients, and enhancing the absorption of nutrients and nutraceuticals in the body;
- developing new sensors for rapid detection of bacteria or viruses, or for "Smart" packaging to sense when a food product has past the use-by time;
- introducing novel surface coatings both to packaging and to processing equipment to give enhanced properties.

The current R&D efforts are largely focusing on high-value products, such as nutraceuticals, interactive and functional foods, etc. These include products that will enable the consumer to modify food depending on choice, needs or tastes. One projected example is a colourless and tasteless beverage that will contain nanoencapsulated ingredients or additives that can be activated by a

[7] Boxall, A.B.A., Chaudhry, Q., Sinclair, C., Jones, A., Aitken, R., Jefferson, B., and Watts, C. (2007). Current and Predicted Environmental Exposure to Engineered Nanoparticles. Central Science Laboratory, York. http://randd.defra.gov.uk/Document.aspx?Document=CB01098_6270_FRP.pdf

consumer at a particular microwave frequency. This would lead to activation of selected nanocapsules while the others remain intact, releasing only the preferred flavour, colour or nutrients (Cientifica, 2006).

Carbon nanotube–polymer composites

Carbon nanotubes (CNT) can be formed as single-wall carbon nanotubes (SWCNTs), or multi-wall carbon nanotubes (MWCNTs). CNTs are elongated tubular structures, typically 1–2 nm in diameter for SWCNTs. They can be produced with very large aspect ratios and can be more than 1 mm in length. CNTs have very high tensile strength, and are considered to be 100 times stronger than steel, whilst being only one-sixth of its weight, making them potentially the strongest, smallest fibre known. They also exhibit high conductivity, high surface area, distinct electronic properties, and potentially high molecular adsorption capacity. Because of the strength they can provide to polymers, SWCNTs are being studied for use as reinforcing agents for intercalation matrices in polymer composites such as PA, polyesters, polycarbonates & blends, PS, polyphenylene sulphide (PPS), PEI and polyether ether ketone (PEEK) for a variety of packaging applications. There is also a possibility of CNT nanocomposites with polyolefins. However, to date, there is no known example where CNTs have been incorporated in an FCM.

Polymer nanocomposite films

Materials being developed as part of "Smart" packaging will incorporate a variety of nano(bio)sensors to monitor the condition of food. These sensors, embedded in polymers, or applied as labels, will be able to detect food pathogens and trigger a colour change in the packaging to alert the consumer to contamination or spoilage. Also under development is the so-called "Electronic Tongue" technology, which is made up of sensor arrays that signal the condition of the food. Other applications under development would repair small holes/tears in packaging and respond to environmental conditions (Garland, 2004).

Polymer composites with nano-encapsulated substances

Current research in this area is examining the potential application of nano-encapsulated substances for antibacterial packaging, and scented packaging. The substances being considered for addition to nanocapsules include enzymes, peptides such as oral vaccines, catalysts, oils, adhesives, polymers, inorganic nanoparticles, latex particles, biological cells, flavour and colour enhancers, or nutritional compounds such as vitamins.

Dirt repellent coatings at nanoscale

Nanostructured coatings for dirt-repellent surfaces have been developed by researchers at the University of Borin. The cleaning action is reported to be due to a "lotus effect" (which refers to the phenomenon that water beads and runs off the surface of lotus leaves owing to nanoscale wax pyramids on the surface of the leaves). The projected applications include self-cleaning surfaces that can help prevent growth of micro-organisms and ensure food safety, such as in abattoirs and meat processing plants (Garland, 2004). Other potential applications could be the development of reusable packaging materials that would enable reduction in the amount of packaging waste.

Nanomaterials for next generation packaging displays

"Smart" labels are being developed with radio frequency identification displays (RFIDs) to enable rapid and accurate distribution of a wide range of products (including foodstuffs) that have a limited shelf-life. Under development are RFIDs incorporating polymeric transistors that use nanoscale organic thin-film technology. The RFID systems will be designed to operate automatically, and will provide exception reports for anomalies in temperature etc. for products with short life span (Garland, 2004). This technology will also improve food authenticity, traceability and food security.

Improvement of the performance of biobased polymers

Biobased polymers can be defined as polymers obtained directly from biomass (polysaccharides, proteins, peptides), polymers synthesized using biobased monomers (e.g. polylactic acid), or polymers produced by micro-organisms (e.g. polyhydroxybutyrate). Most biobased polymers are also

biodegradable. Typically, the use of biodegradadable polymers as food packaging materials has so far been limited, because of inferior performance compared to synthetic plastics. These include poor mechanical strength, high permeability to gases and water vapour, low heat distortion temperature, and poor resistance to protracted processing operations (Sorrentino *et al*., 2007). However, the interest in biodegradable polymers has increased in recent years because of environmental considerations. This is an emerging area of R&D with potential application of nanotechnologies to improve the properties of the biodegradable polymers. The potential developments in bionanocomposites for food packaging applications have been reviewed by Sorrentino *et al.* (2007). A typical example is that of polylactic acid (PLA), which is a biodegradable thermoplastic polyester that has a high mechanical strength but low thermal stability and low water vapour and gas barrier properties, when compared with synthetic polyolefins and polyesters. Unmodified PLA is used in applications where these limitations are not critical, such as for yoghurt pots and as a water-resistant plastic layer in compostable paper cups for beverages. The incorporation of 5 percent (w/w) of montmorillonite into PLA has been reported to improve tensile modulus and yield strength, along with a reduction in the oxygen permeability (Akbari *et al*., 2007).

Similarly, starch-based polymers form a poor moisture barrier and have inferior mechanical properties when compared with synthetic plastic films. The incorporation of nanoclay in starch polymers has been reported to improve the moisture barrier and mechanical properties of biodegradable polymers as well as the thermal stability and reduced water absorption of the composite system. For example, Cyras *et al.* (2008) and Tang *et al.* (2008) studied the effect of adding nanosilica (SiO_2) to starch/polyvinyl alcohol films. They found that addition of nanosilica not only improved the material properties, but that this also had no significant negative effect on the biodegradability of the films.

Nanotechnology has also opened the way for the introduction of other functionalities, such as antimicrobial activity in biodegradable materials. For instance, the preservative benzoic acid has been bonded to a magnesium–aluminium hydrotalcite and the complex has been blended with polycaprolactone to slow down the release of the antimicrobial molecule (Sorrentino *et al*., 2007). Other developments include the use of certain enzymes with antimicrobial activity, which could be covalently immobilized on to amino- or carboxyl- plasma-activated bioriented polypropylene films via suitable coupling agents (Vartiainen *et al*., 2005a).

Another example is the development of bio(nano)composite materials that are based on nanocellulose derived from forestry materials and residues from crop production. The potential applications of the bio(nano)composites will include packaging.

The introduction of ENMs into biodegradable and potentially edible films may lead to increased exposure through ingestion or through the environment.

2.9 Summary

As in other sectors, the advent of nanotechnology offers a wide range of opportunities for the development of innovative products and applications in agriculture, and in food production, processing, preservation and packaging. This chapter has provided an overview of the state of the art with regard to the enormous potential for innovations that nanotechnology applications can bring to the agriculture and food sectors, with many potential benefits to the industry and consumers alike. However, many of the applications are currently at an elementary stage, and as with any new technology, most are aimed at high-value products, at least in the short term. A number of nanotechnology-based food and health food products, and food packaging materials, are available to consumers in certain countries. A further range of materials, products and applications are at different stages of R&D, and some of them may be nearing the market. In view of such developments, it is widely expected that nanotechnology-derived food products will be available increasingly to consumers worldwide in the coming years.

3 Assessment of human health risks associated with the use of nanotechnologies and nanomaterials in the food and agriculture sectors

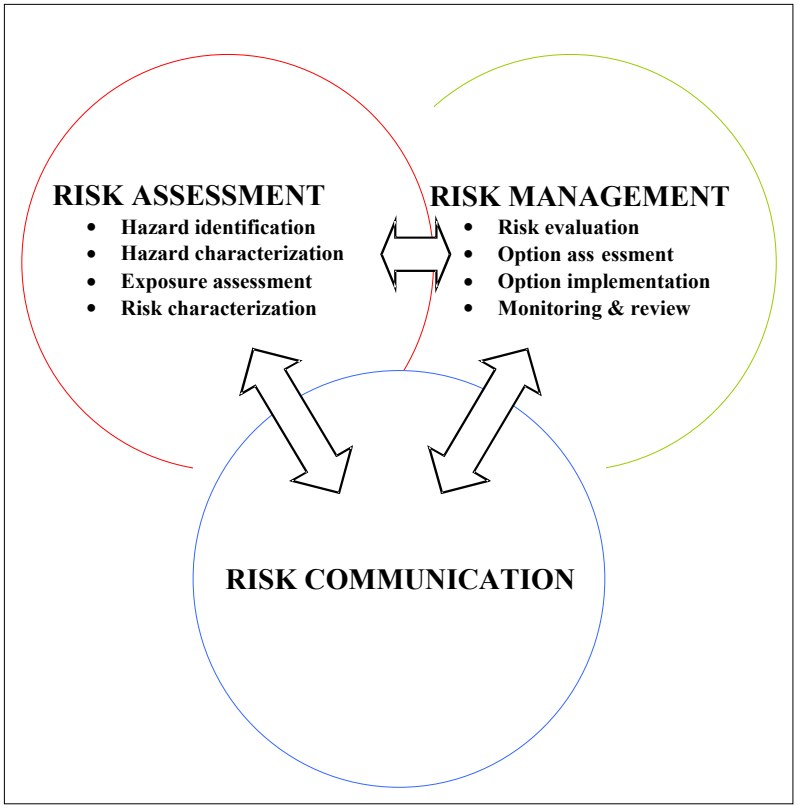
3.1 Introduction

Risk assessment (RA) is a scientific approach to estimating a risk and understanding the factors that influence it. Starting with problem formulation, the process comprises four elements: hazard identification, exposure assessment, hazard characterization and risk characterization (Codex, 2007b; FAO/WHO, 1995a; 1997; SSC, 2000). Hazard identification consists of identifying known or potential adverse health effects in humans that are associated with exposure to a biological, physical or chemical agent (FAO/WHO, 1995). Hazard characterization includes the qualitative and/or quantitative evaluation of the nature of the adverse effects associated with the agent; if sufficient data are obtainable, a dose–response assessment should be performed (FAO/WHO, 1995). Exposure assessment involves the qualitative and/or quantitative evaluation of the likely intake of the agent via food as well as exposures from other sources if relevant (Codex, 2007). Risk characterization integrates hazard identification, hazard characterization and exposure assessment into an estimation of the adverse effects likely to occur in a given population, including the uncertainties (FAO/WHO, 1995).

While the traditional RA paradigm is considered generally appropriate for engineered nanomaterials, it is also clear that additional safety concerns may arise due to the nanocharacteristics of ENMs (COT, 2005; 2007; SCENIHR, 2006; 2007a). It needs to be recognized that the (toxicological) work that has been done so far addresses primarily the occupational hazards associated with the manufacture and handling of nanostructured materials. Much less is known regarding the behaviour and fate of ENMs in the gastrointestinal tract.

In the subsequent sections the appropriateness for ENMs of each stage of the risk assessment paradigm will be discussed.

Figure 1. Risk analysis framework (FAO/WHO, 1997)



3.2 Problem identification

Professional publications, as well as reports in the popular media, suggest that the number of products incorporating nanomaterials or resulting from nanoscience- and/or nanotechnology-based food or feed processes is growing exponentially. At the same time, some corporate sponsors of such products have decided to avoid any reference to "nano" in their communications as a reaction to public concerns. With regard to the development of applications, food technologists in industry and academia – and, in some instances, in joint industry–academia consortia – have manifested interest as early as 2002. In response to public concern, large food corporations have made their interest in nanotechnologies less visible.

With respect to risk assessment and safety evaluation, again, both industry and academia share a strong interest, motivated by consumer safety and confidence as well as avoiding sales revenue losses associated with actual or merely perceived risks in a low profit margin/high volume business. This points to a set of key issues; namely, a likely increase in public and environmental exposure, a documented public concern stemming from hearing scientists acknowledge data gaps and learning about the availability of an increasing number of products, a perceived lack of transparency – or, at least, some incoherence – in corporate communication, and a general dissatisfaction with the global, societal governance on nanotechnologies.

Finally, public authorities are in the process of developing policy in the form of advisories, voluntary schemes, and, in some instances, legislation without either qualified, reliable estimates of risks or availability of methods, instruments and resources to evaluate them. This situation requires urgent progress in the risk assessment of products

Examples or case studies of completed safety evaluations highlight the challenges and lessons learned as well as the uncertainties. Few completed case studies were found that address nanotechnologies in food and agriculture. A set of case studies on hypothetical food contact materials was completed in a joint effort by the Woodrow Wilson Institute Project on Emerging Nanotechnologies and the Grocery Manufacturers Association (Taylor, 2008). This document frames questions that need to be addressed in risk assessments. Case studies for six agricultural applications of nanotechnology and the risk issues posed are discussed in Kuzma *et al.* (2008), but a completed risk assessment is not included. The International Risk Governance Council (2008) also provides a brief overview of the challenges associated with applying the risk assessment framework to three nanoparticles used in food and cosmetics. The risk analysis framework proposed jointly by the Environmental Defense Fund and DuPont (Environmental Defense Fund–DuPont Nano Partnership, 2007) has been applied to a nanoscale titanium dioxide used in food and beverage containers as an inorganic light stabilizer (DuPont, 2007).

The meeting identified two case studies (Appendix 5). Beta-cyclodextrin, a substance that meets the definition of an engineered organic nanomaterial, was developed as a carrier for single molecules such as vitamins or flavourings more than 20 years ago, and has been evaluated as a food additive and ingredient by several scientific bodies, among them JECFA (WHO, 1995). A second hypothetical case study is zinc oxide used as an antimicrobial in food packaging.

3.3 Risk assessment: Hazard identification

What makes ENMs special is that as the size of the particles decreases, the specific surface area increases in a manner inversely proportional to their size, until the properties of the surface molecules dominate, resulting in novel properties determined by the high surface-to-volume ratios. Besides offering a wide range of novel applications, this may also give rise to altered kinetics and toxicity profiles. The very high surface area of ENMs may have several consequences that need to be considered in RA contexts, because it makes them different from their micro/macroscale counterparts. For example, they have increased (surface) reactivity compared with the non-nanoscale material, because many more molecules may be located at the surface in energetically unstable states. Many

types of ENMs catalyse reactions, mainly oxidation reactions. They may also act as nuclei in heterogeneous nucleation processes during crystallization and recrystallization in material sciences (and potentially modifying the secondary or tertiary conformation of proteins). ENMs in food may encompass many forms and undergo dynamic changes in response to their environment. Free ENMs (also referred to as primary ENMs) tend to agglomerate, resulting in bigger particles (secondary ENMs), which may preserve some of the nanoscale properties, such as high surface area and reactivity. The tendency of ENMs to agglomerate can be enhanced or hindered by the modification of the surface, for example in the presence of chemical agents (e.g. coatings, surfactants, ions). Principal physicochemical parameters for the characterization of ENMs are size (including its distribution), shape (including aspect ratios where appropriate), chemical composition, surface area and the morphological substructure of the substance. Other parameters include surface charge and surface coating, chemical reactivity and the presence of contaminants derived from their synthesis or preparation. In addition, properties such as solubility and/or corrodibility are important when ENMs are applied in food. Several comprehensive publications on the properties and characteristics of ENMs have been published recently (Balbus *et al.*, 2007; ICON 2008; OECD, 2008a, b; Rose *et al.*, 2007; Simon and Joner, 2008a).

Owing to their specific physicochemical properties, it is to be expected that nanoparticles could interact with proteins, lipids, carbohydrates, nucleic acids, ions, minerals and water in food, feed and biological tissues. Therefore, it is important that the effects and interactions of ENMs are characterized in the relevant food matrix (Gatti *et al*., 2009; Oberdorster *et al*., 2005b; Powers *et al*., 2006).

Techniques characterizing physicochemical properties

A complete and accurate characterization of ENMs (Oberdorster *et al.*, 2005a; Powers *et al*., 2006) is an essential part of understanding both the possible benefits and the potential toxicity of nanoparticles (NPs) in biological systems (Royal Society, 2004). Whereas the characterization of chemicals is usually relatively straightforward (e.g. composition, purity), characterization of nanoparticles in biological matrices is more complex from an analytical point of view, but also regarding a lack of knowledge about which characteristics need to be identified (Powers *et al*., 2006). It may, however, not always be possible to characterize the nanoparticles fully. In an attempt to give some guidance on prioritization of characterization of nanoparticles, Oberdorster *et al.* (2005a) proposed three criteria:

- the context within which a material is being evaluated;
- the importance of measuring a specific parameter within that context;
- the feasibility of measuring the parameter within a specific context.

At present there is a vast array of analytical techniques to characterize Nanoparticles (Oberdorster *et al*., 2005a; Powers *et al*., 2006; Thomas and Sayre, 2005; Tiede *et al*., 2008), but methods for *in situ* characterization of nanoparticles are currently lacking, as are methods for the detection of nanodelivery systems (Luykx *et al*., 2008). Therefore, priority research should focus on methods that are capable of *in situ* detection and characterization of nanoparticles, ideally using methods that are relatively easily performed with equipment that is present currently in laboratories suited to detection of chemicals in food.

Characterization must verify parameters such as size (in nm), morphology (spherical, rods, cubic, etc.), chemical composition, surface charge and surface coating, chemical reactivity, and presence of contaminants derived from synthesis or preparation. Important parameters for use in the food industry are solubility and/or corrodibility, because it is mandatory that they are biodegradable in human or animal bodies. The biopersistance of dry or wet ENM means their lack of digestibility, a factor that can induce adverse biological effects because they can form foreign bodies.

A non-exhaustive list of equipment required to characterize ENMs includes: SEM (scanning electron microscope), TEM (transmission electron microscope), ESEM (environmental scanning electron microscope), FEG-ESEM (field emission gun–environmental scanning electron microscope), EDS (energy dispersive system), XRD (X-ray diffractometry) and dynamic light scattering (DLS). UV-Vis

(ultraviolet–visible spectroscopy) can be used for the physical and chemical characterization of size, morphology, chemical composition, and crystallinity.

For colloidal ENM, in wet solution, other characteristics must be verified such as: concentration ENM molarity (in μM), mass in μg/ml, pH of the solution, optical or magnetic properties, range of sizes, ENM dispersion in the medium and size range with DLS or Zeta potential, and cohesion forces (that lead to ENM agglomeration). More sophisticated equipment is necessary to verify interaction of the ENM with the matrix.

Interaction of nanomaterials with biology

Bio-kinetics: Biokinetics deals with absorption, distribution, metabolism (biotransformation) and excretion/elimination (ADME) of substances in the body. This whole cascade of events, which occurs following ingestion, determines the internal exposure of organs to potentially toxic substances. Nanoparticles may pass the epithelial barrier lining the digestive tract. After passage through the epithelium, either across cells or via endocytosis, nanoparticles can enter the capillaries and can appear in either the systemic circulation or the portal circulation to the liver. Alternatively, they may be delivered to the lymphatic system, which empties via the thoracic duct into the systemic blood circulation. Translocation of particles through the wall of the digestive tract is a multi-step process, involving diffusion through the mucus lining the GI tract wall, contact with enterocytes or M-cells, cellular or paracellular transport, and post-translocation events (des Rieux *et al*., 2006; Hoet *et al*., 2004).

The properties that make ENM unique are also the properties that are important for risk assessment (SCENIHR, 2006). The experimental data available so far indicate that the characteristics of nanoparticles are likely to influence their ADME (Ballou *et al*., 2004; des Rieux *et al*., 2006; Florence, 2005; Jani *et al*., 1990; Roszek *et al*., 2005; Singh *et al*., 2006).

An important property of ENMs is their interaction with proteins (Cedervall *et al.*, 2007a; Lynch and Dawson, 2008). Protein adsorption to ENMs may enhance membrane crossing and cellular penetration (John *et al.*, 2001; 2003; Panté and Kann, 2002). Furthermore, interaction with ENMs may affect the tertiary structure of a protein, resulting in malfunctioning (Lynch *et al.*, 2006). Such ENM–protein interactions may not be static but may change over time (Cedervall *et al.*, 2007a; 2007b).

Only limited information is available on the absorption of ENMs following oral administration. Gold nanoparticles (Au-NP) (58, 28, 10 and 4 nm) that were fed to mice showed increased GI uptake with diminishing size (Hillyer and Albrecht, 2001). In a study using I^{125} labelled polystyrene ENMs ranging from 50 to 3000 nm in rats, Jani *et al.* (1990) found 34 percent of the label on the 50 nm nanoparticles to have been translocated. However, their conclusion that this represents translocation of the nanoparticles has to be viewed with caution, given that the label was not stable, which resulted in significant urinary excretion that needed to be corrected for.

Titanium dioxide (TiO_2) particles as large as 500 nm (nominal diameter) have been found to be absorbed, with 5 percent of the administered dose absorbed after repeated oral gavage administration for 10 days to rats (Jani *et al.*, 1994). In contrast, for much smaller TiO_2 particles (25, 80 and 155 nm), only minute percentages were reported 14 days after administration of single doses of TiO_2 to mice (Wang *et al.,* 2007a). However in this paper the characterization of the particles was insufficient and the administered dose (5 g/kg body weight) was high.

The GI absorption of ENMs may be affected by different surface coatings, as shown for detergent coated polymethyl methacrylate (130±30 nm) administered by oral gavage to rats. While the uptake was increased by the surface coating, total absoprion ranged from 1 to 3 percent (Araujo *et al.*, 1999). Degradation of poly(D,L-lactic acid) nanoparticles (95 and 150 nm) in the GI tract when administered by gavage to guinea pigs was reduced by coating the particles with albumin or polyvinylalcohol (Landry *et al.*, 1998). The biokinetics of beta-cyclodextrin have been evaluated by JECFA (1995).

Unfortunately, there is little information regarding the distribution of nanoparticles following oral exposure (Hagens *et al*., 2007). In a 28-day oral study of 60 nm silver nanoparticles (Ag-NP) in rats, the highest Ag levels occurred in the stomach, followed by the kidney and liver, lungs, testes, brain and blood (Kim *et al.*, 2008). Silver levels in the kidneys were, for all doses, twice as high in female rats as in males. The distribution was dependent upon particle size. With administration of gold nanoparticles (Au-NP) (58, 28, 10 and 4 nm) to mice, smaller particle size resulted in increased distribution to organs (Hillyer and Albrecht, 2001). If surface area is considered instead of mass, the impact of small size is greater. The smallest particles were found in kidney, liver, spleen, lungs and brain, while the largest remained almost solely inside the GI tract. Uptake of labelled polystyrene ENMs (50 nm) as high as about 7 percent was found in a composite of liver, spleen, blood and bone marrow (Jani *et al.*, 1990). However, the stability of the label was not corrected for.

Preferential retention of large particles in the GI tract was also shown with 500 nm (nominal diameter) TiO_2 particles, which were present in Peyer's patches and the mesenteric lymph nodes (Jani *et al.*, 1994). However, there was systemic distribution, and TiO_2 particles were detected in lung and peritoneal tissues, but not in heart or kidney. By chemical analysis Ti could be detected in liver, lungs, spleen, heart and kidney – however, chemical detection does not provide information on the actual size of the particles.

Information on the potential of nanoparticles to cross natural barriers such as the cellular, blood–brain, placenta and blood–milk barriers are important for hazard identification. However, in some cases, it is technically impossible to identify the particle size after crossing of biological barriers. The technical uncertainties should be taken into account when assessing the potential for absorption and distribution.

Very little is known regarding the biotransformation of nanoparticles after oral administration. The metabolism of nanoparticles should depend, among other properties, on their surface chemical composition. Polymeric nanoparticles can be designed to be biodegradable. The degree of dissolution of nanoparticles will be of importance. Even less is known about the excretion of nanoparticles. As indicated, the potency of nanoparticles to interact with normal food constituents has raised speculation whether some nanoparticles may act as carriers (a "Trojan horse" effect) of contaminants or foreign substances present in food (Shipley *et al*., 2008). This could contribute to exposure to these compounds, with potential implications for consumer health. Nanoparticles have been detected in certain organs of the human body using environmental scanning electron microscopy (ESEM) (Gatti and Montanari, 2008).

Toxicological effects

Some substances that would be captured under the current broad definition of ENM have been characterized extensively toxicologically and have been used safely over a protracted period of time. Examples of such materials include some cyclodextrins, other large structured molecules and polymers and fumed silicon dioxide. Equally, a range of nanomaterials used in the pharmaceutical industry as modifiers of drug pharmacokinetics, liposomes, nanoemulsions and micelles in particular, have also been studied extensively in both experimental animals and humans without evidence of unusual toxicity despite parenteral administration, and are used as delivery systems for approved pharmaceutical products. Examples include: micelles (Taxol®, Konakion MM®, valium MM®), submicron emulsions (Diazemuls®, Diprivan®, Intralipid®) and liposomes (Ambisome®, Doxil®, Visudyne®). Summaries of the clinical and safety data submitted and assessed in support of these nanomaterials can be found at (see drugs at FDA[8] and EMEA[9]).

Knowledge of the potential toxicity of some classes of ENMs, such as nanoparticles with specific surface properties, is limited but growing rapidly. Most of the work that has been done so far addresses primarily the occupational hazards associated with the manufacture and handling of nanostructured materials. There is a body of review papers available (Donaldson *et al.,* 2001; Gatti *et*

[8] http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA/
[9] http://www.emea.europa.eu/htms/human/epar/eparintro.htm

al., 2008a, 2008b; Hansen *et al*., 2006; Nel *et al*., 2006; Oberdorster *et al*., 2005a; 2007) that suggest that, owing to their increased specific surface area and potentially altered bio-kinetics, nanoparticles may have a toxicity profile that deviates from that of their bulk equivalents. The toxicity of the nanomaterial, however, may be less than, greater than or similar to that of the bulk material, depending on the characteristics both of the material of which it is composed and of the particle itself (EFSA, 2009). The relationship between the nanomaterial and the bulk material may depend on the dose metrics used in the comparison.

There are only a limited number of published oral toxicity studies on some classes of ENMs, with those on solid particulates largely limited to insoluble metals and metal oxides. The quality of many of these studies is questionable, severely limiting the use of this information for risk assessment purposes (EFSA, 2009). Common limitations include: use of a single size of ENM, poorly characterized ENM, administration of ENMs at unrealistically high doses, study of only a narrow range of biological parameters, or omission of an appropriate larger particle of the same composition and a soluble form of the parent material as comparators to allow distinction between the effects of particle sizes and those of release of particle surface material into solution (Oberdorster *et al*., 2007). This leads to the conclusion that the current state of knowledge does not permit reliable prediction of the toxicological characteristics of any given ENM from data on other ENMs or from a consideration of the characteristics of the ENM itself. The capacity to predict computationally (e.g. using QSAR) the toxicological properties of conventional materials, however, although considerably greater than for ENMs, is nonetheless limited and of variable reliability.

It is not only the ENM itself that may trigger biological effects. ENMs may absorb or bind proteins or other compounds on their surfaces (Lynch and Dawson, 2008; Simon and Joner, 2008), and act as carriers of these substances into the organism, and indeed many ENMs have been or are being designed for this specific purpose. This selective binding and carrier potential has been termed a "Trojan horse" effect (EFSA, 2009). The use of a nanocarrier to increase the bioavailability of bioactive compounds raises similar issues. The suggestion is that these carrier systems might impact the absorption of molecules, for example by introducing unintended molecules such as undigested or unmetabolized compounds across the GI tract, leading to unintended effects. For example, chitosan can adsorb fat, including fat soluable micronutrients, and thereby prevent their absorption in the GI (Alkhamis *et al*., 2009). These issues, and the potential to disrupt the GI barrier, will need to be addressed during the safety assessment of ENMs that have this potential, and in particular will require a careful consideration of the biokinetics and binding characteristics of the ENM under consideration.

In vitro and in vivo testing

Testing systems: One of the most important questions for the safety assessment is the sensitivity and validity of currently used test assays (e.g. as in the OECD guidelines). A range of ENMs, such as large molecules and liposomes, have been studied successfully using these or similar protocols but studies on structured nanoparticulates are more limited. Thus, while the knowledge on potential toxicity of nanoparticles is growing, so far oral studies are limited to acute dosing (single dose). There is a great demand for studies using chronic oral exposure to nanoparticles combined with a broad screen for potential effects. Information from toxicity studies with other routes of exposure indicate that several systemic effects on different organ systems may occur after long-term exposure to some nanoparticles, including on the immune, inflammatory and cardiovascular systems. Long-term oral exposure studies have not been conducted. Effects on the immune and inflammatory systems may include oxidative stress and/or activation of pro-inflammatory cytokines in the lungs, liver, heart and brain (Gatti and Montanari, 2008). Effects on the cardiovascular system may include pro-thrombotic effects and adverse effects on cardiac function (acute myocardial infarction and adverse effects on the heart rate). No data on genotoxicity, or on possible carcinogenesis and teratogenicity, is available for nanoparticulates as yet (Bouwmeester *et al.*, 2009). The potential for long-term effects will depend at least in part on the rate of biodegradation within the organism and therefore the biopersistence of particulates, coupled with the pattern of distribution and efficiency of elimination.

As for conventional substances, when evaluating the plethora of *in vitro* studies on nanoparticles, caution has to be exercised when extrapolating their results or mechanisms for hazard characterization to subsequent risk assessment in humans (Oberdorster *et al*., 2007). Typical problems with the published literature on *in vitro* studies on ENMs have been the administration of physiologically non-relevant doses and dose rates, aggregation of particles, direct exposure of cells to the ENMs, as well as interpretation of the results. The *in vitro* studies might, however, be suitable for exploring mechanistic explanations of toxic effects, or as screening methods in combination with profiling studies in a tiered hazard assessment approach (Balbus *et al*., 2007; Lewinski *et al*., 2008). A common finding in the *in vitro* assays on nanoparticles seems to be the generation of reactive oxygen species (Balbus *et al.*, 2007; Chen *et al.*, 2008; Donaldson and Borm, 2004; Lewinski *et al.*, 2008; Nel *et al.*, 2006; Oberdorster *et al.*, 2005b; Peters *et al*., 2007).

Dose metrics: When describing the dose–response relationships of ENMs, several interrelated dose metrics have to be considered; namely, mass, number and surface area. Although studies with nanoparticles have shown that for a given nanoparticle any of these can be used to establish observed responses. This is not the case when comparing responses between different types of nanoparticles. Therefore, reporting mass doses alone as a metric is not sufficient in isolation because it does not incorporate the specific characteristics of ENMs (SCENIHR, 2006; SCENIHR, 2007a). Studies by several groups have shown that nanoparticle surface area, rather than mass or number, is the more appropriate dose metric when comparing different types of nanoparticles (Donaldson *et al*., 2001; Duffin *et al*., 2002; Oberdorster *et al.*, 2007).

Thus, it is obviously desirable to characterize EMNs as completely as possible (Oberdorster *et al.*, 2005a; OECD, 2008b; Powers *et al.*, 2006; Thomas and Sayre, 2005) with respect to specific surface area and number concentration per mass in order to establish dose–response relationships. Considering that, for poorly soluble ENMs, chemical reactivity as well as biological activity are dependent upon surface characteristics, another surface-related dose metric, i.e. surface reactivity, should be considered as a dose metric in future studies.

Clinical studies: Only very limited human clinical data was found by the working group. Two human studies exist that evaluate the bioavailability of fat-soluble substances (vitamin E, coenzyme Q10) encapsulated in hydrophylic nanoparticles, compared with oily solutions or crystalline preparations. The nanoparticle associated CoQ10 showed an earlier flooding compared with oily dispersions and crystalline CoQ10, resulting in significantly elevated area under the curve (AUC) between 0 and 4 hours but not between 0 and 12 hours. Long-term supplementation resulted in significantly higher plasma levels for all formulations with nano-encapsulated CoQ10 compared with the other preparations (Schulz *et al*., 2006; Wajda *et al*., 2007). In a clinical trial the bioavailability of vitaminized jelly bears with nano-encapsulated vitamin E was evaluated against conventional preparations (Back *et al*., 2006). The AUCs (0–320 minutes) of nano-encapsulated alpha-tocopherol were significantly larger ($p = 0.016$) when compared with the conventional product. Differences in bioavailability when using nanoparticles to transport fat-soluble micronutrients need further studies to determine the effectiveness of this approach, in particular in groups suffering from fat malabsorption.

3.4 Hazard characterization

Owing to the considerable uncertainties regarding both extrapolation from toxicity information on bulk materials to nanomaterials and interpolation within the limited toxicity data available on nanomaterials, hazard characterization may be the most problematic part of risk assessment of nanomaterials where direct studies are not available. Initially, until data can be developed and shared to produce a broader understanding of variations in toxicological effects in relation to the range of characteristics of nanoparticles, hazard assessment will need to be on a case by case basis. Some general rules have been suggested for individual assessments (SCENIHR, 2007), based on the ability to extrapolate from existing data on bulk materials using ADME information. When such

extrapolations cannot be made easily, hazard characterization is likely to require the development of ADME and toxicity data on the material of interest and the expected route of exposure.

Dose–response considerations

For derivation of the NOELs or benchmark doses in order to characterize the risk, especially for regulatory use, *in vivo* toxicological studies should normally be conducted by using a mass-based dose metric. However, the dose–response relationship for nanomaterials in the body is more likely to be described by the physicochemical parameters, such as surface area, size and surface charge, than by mass-based measurement of dose. To evaluate properly the dose–response relationship between the administered dose and the biological effects, kinetic analyses for converting between the *in vivo* dose metric and other significant physicochemical parameters in relation to the responses should be developed, in addition to the controllable dose administration methods. These analyses could be also help to introduce the results of *in vitro* studies into the dose–response assessment. However, there are limitations on the detection, analysis and characterization of nanomaterials in biological systems after absorption, as well as in complex matrices of the administration vehicle. In addition, in some cases, the physicochemical parameters of nanomaterials, such as particle size and surface charge, may differ before and after absorbtion into the body. Such uncertainties should be taken into account in the dose–response assessment in addition to the uncertainties inherent in inter- and intra-species differences.

Species differences in toxicokinetics and toxicodynamics specific to nanoparticles

Given the paucity of data on the toxicokinetics and toxicodynamics of orally administered nanoparticles in general, very little can be said regarding potential species differences. However, it is clear that testing models should be chosen carefully to ensure that human exposure is modelled as well as possible, considering the current knowledge base and especially sensitivity to the most serious potential mechanisms of action of nanoparticles.

Epidemiological studies

Much of the published epidemiological work on nanoparticles and other ENM has focused on exposure through the inhalation route (Oberdörster *et al*., 2005; SCENIHR, 2006). Epidemiological studies were not found for ENM in food after an extensive search of the literature. Epidemiological studies of naturally occurring nanoparticles in food also were not found, although consumption of some natural nanoparticles has been documented since ancient times (Carretaro, 2002; Wilson, 2003).

Exposure assessment

The use of nanotechnologies in the food or agriculture sectors may result in human exposure to engineered nanomaterials. Exposure to nanomaterials in the diet is not new: humans have been exposed to nanomaterials historically, e.g. titanium dioxide and silica nanoparticles (Murr, 2009); clay and soot (Nowack and Bucheli, 2007); aquatic colloids (Ju-Nam and Lead, 2008). Distinguishing between natural and engineered nanoparticles in food and other media will present a challenge for estimating dietary exposure (Tiede *et al*., 2008).

In the food sector, ENMs may be used in processing equipment, food packaging, food contact materials, or used directly in foods and beverages (Sozer and Kokini, 2009). Use of ENMs in the agriculture sector includes the use of ENM in feed (Spriull, 2006), in veterinary medicines (Ochoa *et al*., 2007), in aquaculture (Kumar *et al*., 2008), as smart delivery systems for pesticides and fertilizers (Mukal *et al*., 2009), as biosensors (FSA, 2008), as plant growth regulators (Choy *et al*., 2007) and the use of plants to synthesize nanoparticles (Gardea-Torresdey *et al*., 2002; 2003). Most of these products are subject to some level of regulatory oversight including pre-market review and approval.

For food additives and FCM, information on the amount of the substance intended for use in food or migrating from FCM into food is ordinarily well defined. In addition, residues from veterinary medical uses and pesticide/herbicides in or on food are used as the basis for developing exposure assessments. These data are generally combined with food consumption data or other use data to estimate consumer dietary exposure conservatively. In contrast, potential environmental exposures to ENM pose greater challenges because of the need to characterize and quantify the material once it is released. Dietary

exposure to ENM from environmental and agricultural sources will also depend upon whether the ENM are available to be taken up in the food chain or transported to water sources.

Not all uses of ENM in food and agriculture will result in exposure, and not all exposure will result in risk. The design and use of ENM may reduce the likelihood of exposure in some instances. Nanoparticles fixed within a medium are less likely to move through the environment and will not result in human exposure while they remain fixed in place (Buzea *et al*., 2007). It should be noted however that these particles may be freed from the medium in which they are embedded if the medium is physically or chemically altered (e.g. as a result of disposal or use), in which case exposure to the nanoparticles is possible.

Human exposure to hazards occurs through inhalation, dermal and oral routes. The oral route is expected to be the most prevalent route for non-occupational exposure to ENM used in the food or agriculture sectors. Oral exposure to ENM has received less attention than the dermal or inhalation pathways where a considerable body of work has been conducted. Consideration of other routes of exposure – inhalation, dermal, contributions to oral via clearance from the respiratory tract via the mucoliary escalator – will be necessary when estimating aggregate exposure from multiple exposure sources including those that originate outside the food and agriculture sectors. Exposure scenarios include exposure through food, beverages or water containing ENM – either intentionally or through migration from elsewhere. These scenarios will force consideration of the stability and potential biotransformation of the substance during food processing or in food.

Unintentional incorporation of ENM into the food chain must also be considered as a human exposure scenario. The agricultural use of ENM may result in the transport of ENM away from the site of application or use, potentially resulting in indirect human exposure via the environment. Accidental release or disposal of ENM from non-agricultural uses may also result in environmental exposure. Incorporation of ENM into the food chain and potential bioaccumulation in some species will need to be examined through monitoring or other studies. Recent studies have demonstrated the uptake, translocation and accumulation of NP in crop plants: fullerenes in rice (Lin and Xing, 2009); iron oxide nanoparticles in pumpkin (Zhu *et al*., 2008); hyperaccumulation of nanoparticle silver by alfalfa and mustard (Harris and Bali, 2008). However, more work needs to be done before assuming similar results for all crop plants and nanoparticles. Aquatic food organisms may be exposed to ENM. Mussels take up natural nanoparticles and accumulate metals bound to nanocolloids (Pan and Wang, 2004). *Daphnia*, a favorite food of some fish, take up some nanoparticles (Zhu *et al*., 2009). ENM may be transferred to higher trophic levels, but it is unclear whether bioaccumulation occurs. Holbrook exposed ciliate protozoans to two types of fluorescent quantum dots; the quantum dots were also found in the rotifer that preyed upon the ciliates in a transfer from one trophic level to another. Thus, exposing the ciliates to quantum dots (QD) resulted in limited bioconcentration in the ciliates and transfer to higher trophic levels (rotifers) in a simple aquatic invertebrate food chain, although the QD were eventually excreted by the rotifers and not bioaccumulated (Holbrook *et al*., 2008).

Quantification or estimation of exposure requires that the unit of measurement match the toxicologically relevant aspects of the ENM. Exposure may be measured by evaluating these and other relevant parameters directly, or by measuring quantities that are related in some way to the aspect of interest. Choosing the appropriate exposure metric is dependent upon the expected effects of the ENM. The metric selected to measure exposure should be consistent with the metric by which the hazard of ENM is characterized. In addition, the measurement or estimation of exposure should be consistent with the spatial and temporal scale over which any adverse effect is characterized in the dose–response assessment. The exposure pattern – duration, intensity and frequency of exposure – should be noted.

Estimation of the fate, transport and biotransformation of ENM will be crucial for exposure assessment. Monitoring studies, as well as models, will provide estimates of ENM in various media (e.g. food, water, crop plants, animals, soil and sediment). Transformation of the ENM must be also be considered, because some forms may be more likely to be mobile than others. Among the transformations to be considered are changes into other chemical forms as well as into other physical

forms. Agglomeration of nanoparticles into larger structures is one example of a physical transformation that may affect transport, fate and hazard (Maynard and Kuempel, 2005). Environmental conditions may influence the transformation and transport of ENM, including conditions within food or FCM. For example, the release of material from delivery systems may be triggered by the appropriate environmental condition (e.g. pH, salt concentration) (Sanguansri and Augustin, 2006), and the presence of a complex mixture of compounds in the GI tract may interact with ingested ENP (Hoet *et al*., 2004).

Monitoring studies will provide "real world" estimates of exposure to ENM and aid in the development of appropriate exposure scenarios, but these studies alone will not provide exposure estimates for circumstances that differ from those in the study. Models or mathematical equations provide a tool with which to make such predictions as well as to estimate future exposure. Existing dietary exposure models estimate exposure in terms of hazard mass per unit body mass by combining per capita daily intake of various foods with expected distributions of chemicals or biological hazards in food. These mass concentration-based models may be amenable to modifications that allow them to estimate the relevant ENM toxicological attributes if mass concentration alone proves inadequate. Some progress along this line has been made in estimating relevant attributes from existing measurements for airborne particles (Maynard, 2002). New fate and transport models may need to be developed to predict the behaviour of nanomaterials in food or in the environment if the relevant toxicological attribute of the ENM (e.g. particle size, surface area, particle shape, porosity or surface chemistry) cannot be estimated using existing mass concentration-based models. The recent study on migration of engineered nanoparticles from FCM, which was based on an evaluation of the average distance travelled by the nanoparticles in the polymer matrix, provides an example of a predictive fate and transport model using physicochemical properties of ENM (Šimon *et al*., 2008).

3.5 Risk characterization

Risk characterization for ENMs would not, in principle, differ from that followed for soluble chemicals or the micro/macroscale material (EFSA, 2009). As with risk characterization for non-nano forms of the same chemical, the use of uncertainty factors for ENMs requires consideration (EFSA, 2009). Characterization of uncertainty may require more rigorous analysis than simply applying uncertainty factors. The toxicological and exposure data are generally less well developed for nanoparticles than for other ENM; characterizing the uncertainty associated with nanoparticles may require special consideration during risk characterization.

3.6 Applicability of the risk assessment paradigm for nanoparticles

The traditional RA paradigm is considered generally appropriate for engineered nanomaterials (ENMs) (SCENIHR, 2006; 2007a; FSA, 2008; COT, 2005; 2007) as well as for ENM in the food and feed sectors (EFSA, 2009). The RA paradigm has also been found applicable to nanoparticles, although some modifications to the methodology used are likely to be necessary (FDA, 2007; SCENHIR, 2005; Council of Canadian Academies, 2008). There needs to be special consideration given to the antimicrobial actions of nanoparticles on normal microflora with consequences for microbial safety, or effects on allergenicity caused by adsorption of protein peptides on nanoparticles ("Trojan horse" effect).

Special tools or approaches required for nanoparticle risk assessment

Improved methods to detect nanoparticles in complex matrices would improve exposure assessments (NEHI, 2008; EFSA, 2009). The United States NNI Research Plan discusses the need to develop computational approaches and models to help bridge the gap between macroscale substances and nanoscale versions. This is a pragmatic approach to addressing some toxicological uncertainties, because requiring completely new testing for all nanoscale materials will certainly slow the beneficial applications of this technology.

Consideration of a tiered risk assessment approach

A tiered approach to ENM risk assessments may prove useful to prioritize the use of resources for generation of new data and risk methodologies. The current state of knowledge about the unique properties of engineered nanomaterials does not permit identifying exact criteria that present "bright lines" for inclusion, or exclusion, for nanospecific risk evaluation. For example, the use of 100 nm as a cutoff point for particle size does not have a biological basis, so one cannot simply assign this as an inclusion or exclusion criterion, such as "if the mean particle size exceeds 100 nm, then no nanospecific testing is necessary". Thus, it may be useful in the RA to consider a breadth of potential properties that may indicate unique biological or physical behaviour that will warrant additional toxicological evaluation.

The first step in a tiered approach is to conduct a preliminary screening evaluation to ask whether the available data on the ENM are sufficient or whether a more detailed evaluation, involving the generation of additional data, is warranted. In this first step we envision the use of a broad range of indicators (both physicochemical and biological). Initial indicators are used to assist the prioritization of further analysis and testing. In the absence of validated test results, this tiered approach may use conservative assumptions to fill data gaps in the risk assessment.

Organizing the data generated from the screening evaluations linking physical/chemical properties, biological behaviour and the associated risk estimates should allow future development of a decision tree approach. Ultimately this might enable the prioritization of types or classes of materials where additional data are likely to be necessary to reduce uncertainties in the risk assessment. In addition, this could eliminate from special consideration those nanomaterials (e.g. naturally occurring nanostructures) that do not raise additional safety concerns.

Table 2. Physicochemical and biological/toxicological indicators

Indicators: Physicochemical	Indicators: Biological/ toxicological
Solubility	Biopersistence
Particle size/size distribution	Bioavailability
Complexity of composition	Biocorona
Surface reactivity	Potential for " Trojan horse"

The meeting recognized in its discussion that the first tier of a possible framework for prioritization will be very useful. A diagram, an attempt at this effort, was drafted; however the meeting agreed that it is necessary to further consider more factors involve in prioritization and/or categorization carefully before developing such an approach. The approach may include a decision tree for identifying those classes of ENMs that require specific attention with respect to data and methods used in their risk assessment.

Product life cycle considerations

It is important to consider life cycle aspects in the assessment of ENM. This means, for example, that the fate in the environment must be analysed to assess indirect human exposure via food. Considerations of these aspects in the risk assessment framework will inform and prioritize exposure pathways and identify changes in the attributes of ENM at different stages of the product life cycle, thus identifying the need for more detailed evaluation of particular life cycles. These considerations are most easily applied to the exposure assessment phase of risk assessment. Incorporating life cycle aspects at this stage will identify the life cycle stages with the greatest potential for human exposure. It will also identify environmental pathways that may result in exposure through the food chain, facilitating a "farm to fork" examination of exposure. Disposal of entities containing ENM, e.g. FCM, food packaging, food and water, may release ENM into the environment, resulting in incorporation into agricultural commodities. Incineration of the ENM may also provide a human (and animal) exposure pathway via incorporation into agricultural products and animal feed. This approach could be used iteratively in a tiered approach to conducting risk assessment.

Residual amounts of ENMs that remain in food producing animals at slaughter may result in exposure to humans through consumption of the food animals. Another illustration is the use of ENM in food packaging material resulting in direct exposure to the ENM in the food packaged by the material if the material is compromised. Secondary human exposure from food could result from disposal of the packaging material in a compost bin and subsequent release of the ENM to the soil with uptake by garden produce.

Several risk assessment frameworks incorporating life cycle thinking have been proposed (e.g. Davis, 2007; DuPont, 2007; Shatkin, 2008). An example is Nano LCRA, an iterative framework that uses existing information to identify life cycle stages during which exposure may occur and then prioritizes research needs; it is iterated when additional data are available. This framework can allow preliminary decision-making under uncertainty, although more uncertainty may necessitate more conservative approaches to risk assessment.

Animal health considerations including food of animal origin and residues in animal tissues

Although this document focuses on human risk assessment some aspects of animal risks are relevant. Intentional exposure of food-producing animals to nanomaterials could include veterinary drugs and biologicals (vaccines), animal feed ingredients, or subcutaneous implantation of identifiers that utilize nanomaterials, for use in traceability.

Unintentional exposure of food-producing animals to nanomaterials could occur through consumption of forage exposed to nanomaterials or grazing on pasture where the plants have been exposed to nanomaterials from fertilizers, pesticides or environmental contamination. In addition, water (for drinking or as a fish habitat) could potentially be a source of nanomaterial exposure.

In veterinary drugs, the main risk assessment question would be to determine whether the residue pattern would be changed or whether new residues might occur. For example, could there be persistance of a nanomaterial carrier? In the case of animal feed additives, the focus of risk assessment would be to target the health of animals and the safety of food products (of animal origin). In the example of nanomaterials used for binding mycotoxins in feed ingredients to prevent mycotoxicosis (YingHua *et al*., 2005), there should be consideration in a risk assessment of any impact on animal health associated with the use of nanomaterials. In addition, any potential effects of residual nanomaterials becoming available in the food, in the case of food-producing animals, should be examined.

Any nanotechnological application in food-producing animals should use a life cycle approach while undertaking RA. That is, as the movement of nanomaterial along the agri-food continuum is examined, the appropriate points for risk assessment interventions would be identified. For persistent nanomaterials in particular, this is an important consideration. Two subgroups of the former OIE Ad Hoc Working Group on Biotechnology have been formed: one group on Vaccinology and the other on Molecular Diagnostics. These two subgroups would give due consideration to any relevant nanotechnology applications in these areas.

3.7 Future needs for the assessment and prevention of human and animal health risks

Databases

- Quality-controlled inventory of products incorporating nanomaterials or resulting from nanoscience- and/or nanotechnology-based food or feed processes based on substantiated, statistically tested claims and random samples of new products likely to stem from nanoscience or the nanotechnologies.
- Quality-controlled, remotely accessible, searchable archives of comparable characterization, toxicological, and exposure information.
- Quality-controlled, remotely accessible, searchable archives of risk assessment and test methods.

- Quality-controlled, remotely accessible, searchable archives of safety equipment and equipment characteristics.

Exposure assessment

- Analytical methods and instruments required to assess the (external) exposure of populations and the (internal) exposure of organs in the body – favouring non-invasive approaches.
- Analytical methods and instruments required to characterize, detect and trace inorganic and organic nanomaterials in food and feed matrices, preferably in a high throughput mode;

Hazard identification and characterization

- Documentation, analysis and prediction of the bioavailability of nanomaterials in the human body and animals as well as their fate (absorption, distribution, metabolism, and excretion through active and passive biokinetic processes).
- Documentation, analysis and prediction of the biokinetic implications of coatings and other means of functionalization.
- Documentation, analysis and prediction of how using nanomaterials may bear on food and feed contamination.
- Methods to assess, understand and predict or infer the toxicity of nanomaterials *in vitro*, *in vivo*, and *in silico* – minimizing animal use whenever possible.
- Methods to assess, understand and predict or infer the stability (conversely, transformation and interaction with other ingredients) of nanomaterials in food and feed over time and under different environmental conditions.

3.8 Summary

Future needs and ways forward to prevent human health risks at international and national levels concern knowledge (scientific and market data), resources (funding for studies, facilities and trained investigators), and processes (international scientific collaboration on characterization, methods design and testing; international, multi-stakeholder collaboration on guidelines development and harmonization; public engagement and societal governance).

Knowledge needs

Indeed, major gaps remain with respect to the characterization of nanomaterials as input into food contact materials or ingredients in food or feed preparations, as well as to the effects of nanoscience- and/or nanotechnology-based food or feed processing technologies on the characteristics of the marketed food or feed product. Hence, focusing first on using the existing data, the first priority resides with sharing of: (i) existing characterization, toxicological and exposure data relevant to risk assessment, (ii) experience with different tests and methods in support of updating standard operating procedures, and (iii) in support of exposure assessment, market intelligence regarding actual and foreseen applications (cf. inventories) differentiating between unverified claims and substantiated actual applications of nanoscience and/or the nanotechnologies to food or feed.

However, the available information will not suffice. Therefore, in addition, academic and other independent scientific institutions should plan and engage in production of high quality, comparable and robust data. This information should not only cater to the needs of specific risk assessments but also to the establishment of relevant, reliable and replicable risk assessment methods – including alternatives to animal testing – and to the international harmonization of guidelines for risk assessment and safety assessments. This fundamental work on advancing the scientific knowledge should not exclude pragmatic, operational considerations, in particular with respect to tiered approaches (cf. decision algorithms) and other strategies aiming at clarifying and simplifying the risk assessment process, and to identifying means to handle incomplete information – to avoid having to assume the highest level of danger and exposure in the absence of data.

Resource needs

Promoting the advancement of science and the development of methods calls for shared, remotely accessible databases on a range of different topics (applications, characterization, toxicology, exposure, reported medical incidents, etc.) and infrastructures. In particular, shared analytical facilities are required. Specifically, testing of products establishing a "nano" claim and products not making such claims that could be "nano" will require funding.

Notwithstanding the vitality of a strong scientific community, academia, industry, public authorities and non-governmental organizations (NGOs) must to be able to call upon the competences of a pool of scientists specifically trained in nanoscience and the nanotechnologies. Given the time that it takes to train people, provisions must be made to ensure that this is the case both in the context of academic teaching institutions and as a part of life long learning.

Process needs

The above implicitly outlines the perceived process needs, namely, (i) strengthening or setting up international scientific collaboration on characterization, methods design and testing focusing on food and feed _ or, at least, making specific provisions for each, (ii) establishing an international, multi-stakeholder, structured, sustained dialogue to develop a set of harmonized guidelines, and (iii) informing and engaging the public and more generally ensuring good, global, governance.

4 Development of transparent and constructive dialogues among stakeholders – Stakeholder confidence

4.1 Stakeholder engagement

The engagement of stakeholders is widely acknowledged as imperative for any emerging or controversial issue, such as the introduction of nanotechnology into foods. Throughout this document, "stakeholders" means, in no particular order, "industries", "the public", "consumer and environmental NGOs" , "trade unions" , "public authorities" and "scientists", as well as other interested or affected parties. However, engagement cannot simply be added to a list of requirements for strategies for managing emerging risks or for policy development. The purpose of engaging stakeholders must be identified in advance, whether it is to educate, gain feedback on ideas, or identify concerns. Stakeholder engagement is resource intensive, so it must be focused on a specific set of objectives. Issues including how engagement will occur, timing relative to key decision points, the format for interactions, who the key stakeholders are, and how information from stakeholders will be considered in decision-making are critical elements to identify and communicate.

4.2 Risk communication in risk analysis frameworks

Table 3. Analytical deliverative frameworks

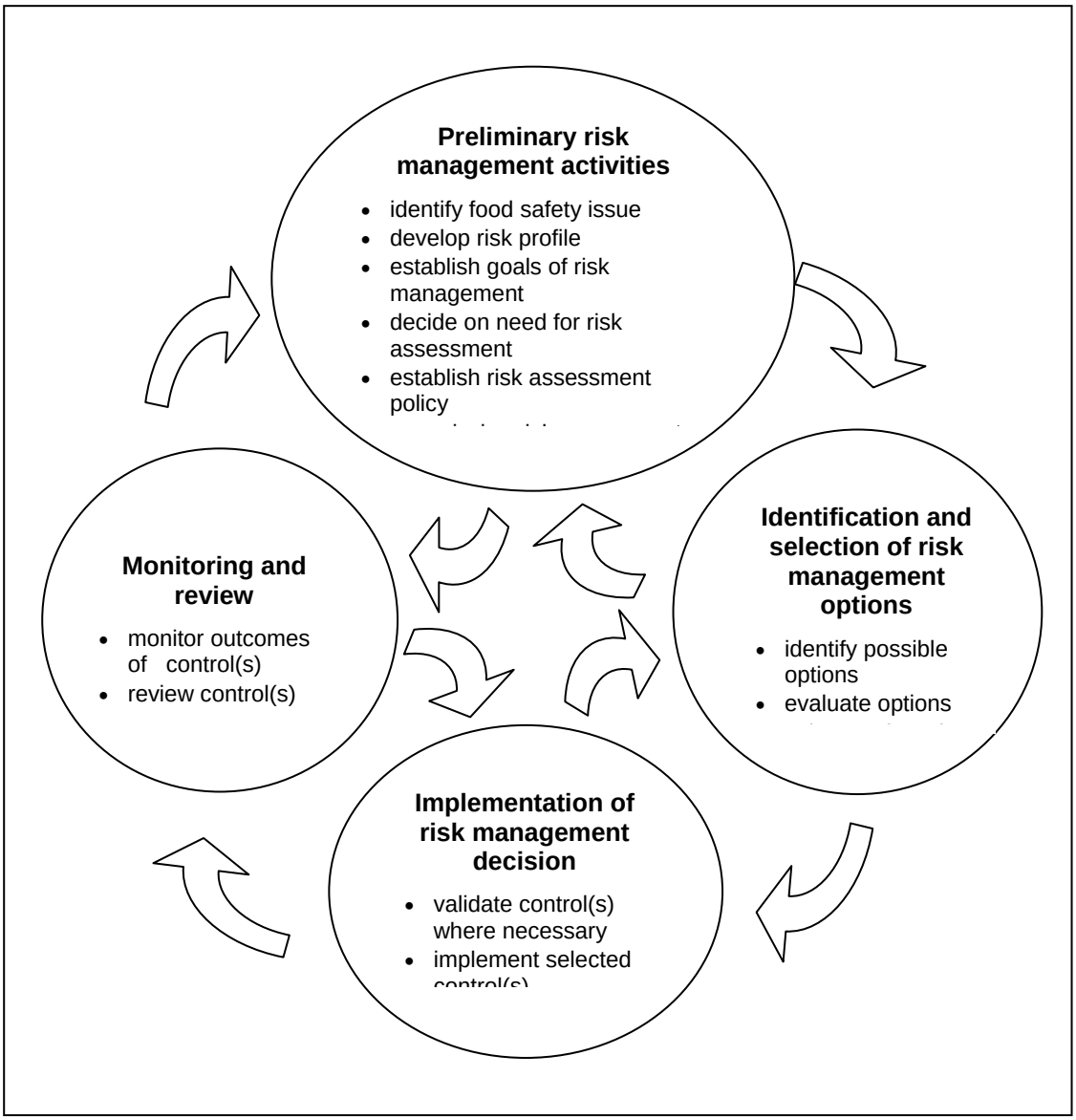
Framework	Features	Reference and Web address
FAO/WHO model	Risk communication and consultation built into international food safety risk framework.	FAO/WHO. 2006. Food and Nutrition Paper 87 http://www.fao.org/docrep/012/a0822e/a0822e00.htm
NRC 1996	Engagement of stakeholders in an analytical-deliberative process to broadly identify and address stakeholder concerns and uncertainty.	*Understanding risk: informing decisions in a democratic society* (1996) www.nap.edu
US Presidential Commission on Risk Assessment and Risk Management in the Federal Government	Proposes engagement model with stakeholders in the centre, consulted at each step of the risk assessment and risk management process, to address key uncertainties in an inclusionary process.	US Presidential Commission on Risk Assessment and Risk Management in the Federal Government. 1997. *Framework for environmental health risk management*. http://www.riskworld.com/nreports/1997/risk-rpt/pdf/EPAJAN.PDF.
IRGC Risk Governance Framework	Includes a concern assessment component of risk analysis, to identify the level of controversy and design adequate stakeholder engagement to address it during the risk assessment process.	IRGC. 2006. *Nanotechnology and risk governance*. White Paper No. 2. Geneva.
SAFE FOODS (NL)	Changes the scope of decision-making on food safety from single risks to considering foods as sources of risks, benefits and costs that are associated with their production and consumption, and taking into account the social context in which decisions are made.	*Promoting food safety through a new integrated risk analysis approach for foods.* http://www.safefoods.nl/default.aspx

The Codex Working Principles for Risk Analysis for Food Safety for Application by Governments (Codex 2007) include specific requirements for risk communication, specifically that the following should be achieved with regard to engaging the public:

- foster public understanding of the process, so as to enhance trust and confidence in the safety of the food supply;
- promote the appropriate involvement of all interested parties;
- exchange information in relation to the concerns of interested parties about the risks associated with food.

Overall, the main purpose of risk communication is "to ensure that all information and opinion required for effective risk management is incorporated into the decision making process." The FAO/WHO *Food safety risk analysis: a guide for national food safety authorities* explains the key elements in risk communication within the FAO/WHO risk management framework, and provides useful guidelines about when and how (and how not to) engage stakeholders. While communication is essential at each step of the risk analysis and risk management process, the framework highlights steps that are critical for engaging external stakeholders, as shown in Figure 2.

Figure 2. Risk communication and the generic risk management framework (RMF)
(Source: FAO, 2006)



In *Understanding risk*, the National Research Council lays out elements of an analytical-deliberative process: getting the science right; getting the right science; getting the right participation; getting the participation right; developing an accurate balanced and informative synthesis. All of this is to say: be clear what problem you are solving, and ensure it is the one that people care about, and that people agree with how you are doing the assessment, what data are used, and how they are interpreted.

Stakeholder engagement is addressed by the 1997 United States Presidential Commission report on risk assessment and risk management, *Framework for environmental health risk management.* The proposed framework for risk management puts stakeholders in the middle of the decision process, engaging their participation at each step of the process. This risk management framework is intended to be broad, to address a range of types of hazards, and to implement an iterative process that revisits the problem and the risk management options.

The Presidential Commission framework recognized the role of uncertainty in risk assessment. "Risk assessors have to use a combination of scientific information and best judgment" (Commission, 1997). Uncertainty is a key attribute of risk. If there were certainty about the impacts of a particular substance, or technology, one would conduct a safety assessment, and establish a definitive safe level. However, with new materials it is rarely certain that all of the relationships between exposure and effect are understood, and assumptions are made to address the inherent uncertainty. That is one main reason to involve stakeholders in decisions about managing risks. Stakeholder values and preferences must be considered in deciding how to manage risks under uncertainty.

The Safe Foods Initiative coordinated by the Netherlands and funded by the EU 6th research monogramme promotes food safety through a new integrated risk analysis approach for foods that changes the scope of decision-making on food safety from single risks to considering foods as sources of risks, benefits and costs that are associated with their production and consumption, and taking into account the social context in which decisions are made.

A recent report, *Risk governance of nanotechnology applications in food and cosmetics* (IRGC, 2008), highlighted the importance of engaging stakeholders around key issues such as terminology and regulatory development, particularly because of the situation of low trust in industry and governments, to protect public health and the environment.

The International Risk Governance Council (IRGC), based in Switzerland, addresses risk governance for emerging risk issues. The IRGC has published a risk governance framework (IRGC, 2005) that has been applied to nanotechnology generally, and has been used to frame the issues for nanotechnology in food and cosmetics. The main contribution of the IRGC framework is the inclusion of the societal context in risk assessment and risk management. In their governance framework, IRGC gives equal weight to the societal dimension of risk management, recognizing that some societal risks are more complex, and of greater concern, than others in a governance model. A major innovation of the IRGC framework is in categorizing risk-related knowledge. Categorization addresses complexity, uncertainty and ambiguity of risks. The IRGC framework also considers risk/risk and risk/benefit trade-offs, such as the risk of complications from surgery (the risks of complications may or may not outweigh the benefits of the surgery).

The IRGC has applied this framework to nanotechnology, describing four generations of nanotechnology and their differences in terms of complexity, uncertainty and ambiguity (IRGC, 2006). The first generation, passive nanostructures, represent those materials that exist or are in development today. The second generation involves active nanostructures, such as smart packaging, or targeted drug delivery. Third generation (self assembling structures), and fourth generation (molecular manufacturing) are viewed as forthcoming. Moving beyond the first generation of types of materials currently applied in nanotechnology, (generally passive nanoscale particles, or substances and structures created at the nanoscale such as silver or gold that are smaller than larger particles, but

remain generally as they were manufactured), complexity, uncertainty and ambiguity increase and risk governance models must adapt (IRGC, 2006).

In 2008, the IRGC examined the issue of nanotechnologies in food and cosmetics. Their report highlights the complexity of the issue of terminology. "The question of what is meant by nanotechnologies and nanomaterials, especially in food and cosmetics, remains one of the key issues of debate between public authorities, industry, scientists, consumers, environmental groups and the media." One of the key findings is that communication about the risks of nanotechnology and nanomaterials is hindered by lack of agreement about definitions, which could lead to misinformation and inconsistencies. Further, the lack of authoritative information about the applications using nanomaterials and nanotechnologies in food, food packaging and agriculture has led to largely speculative discussions about uses and potential risks. The authors highlight the need for a "balanced and concerted dialogue" among stakeholders in private, civil and public sectors on international, regional and local levels to address the pressing need for proactive communication about risks, given the sensitivity of the situation. The low level of public understanding, in combination with the direct exposure pathway of nanotechnology in food (i.e. that it is ingested by people), the perception of inadequate regulatory oversight and a low level of trust in industry create a volatile situation that warrants a concern assessment – analysis of the associations and perceived consequences (benefits and risks) that stakeholders, individuals, groups or different cultures may associate with it – to inform future risk characterization and evaluation.

4.3 Models of Engaging Stakeholders

Risk communication comes in many forms. For example, it can include information presented in print or visual media, interactive fora with experts and stakeholders, public hearings about regulatory decisions, and public participation methodologies, among many other activities. Informing, negotiating and deliberating are activities within risk communication. Strategies for risk communication will vary depending on cultural and political contexts, responsible or host organizations, available resources and goals. In situations of high uncertainty or ambiguity, with widespread impacts on stakeholders, risk analysis frameworks have emphasized bi-directional communication and learning through engaged models of communication (IRGC, 2006; NRC, 1996).

Rowe and Frewer (2000) broadly review more engaged models such as consensus conferences, citizen juries and focus groups, and evaluate them with two sets of criteria: acceptance and process criteria. "Acceptance criteria" include the representativeness of the participants, independence of participants, the timing of involvement, the potential for influence on the final decision or policy, and the transparency of the process to the public. "Process criteria" include resource accessibility, task definition and cost-effectiveness. Organizations responsible for hosting or initiating risk communication activities will need to consider the assortment of methods and which criteria are most important to them and the stakeholders with whom they engage. There is not a one-size-fits-all approach for risk communication surrounding agricultural and food nanotechnology.

It is important to define clearly the nature, scope, procedures and expected outcomes of risk communication to all the participants at the outset. The effectiveness and credibility of the process thus can be improved. One should recognize that such a rigid criterion may draw the objection of being overly prescriptive and lacking in flexibility should new information emerge that may lead to dispute. Hence, it may be necessary to explain in the terms of reference that an exercise should be allowed to take place in the face of important new information (Rowe and Frewer, 2000).

Effective public engagement requires adequate planning and resources to ensure broad participation and meaningful outcomes. Formal mechanisms for obtaining and responding to concerns and other demands are critical components. Outreach and communications must include an educational component to ensure that all participants are informed about the technical, regulatory and broader societal issues.

However, it remains critical that mechanisms for incorporating the issues raised by participants are explicit and are followed. All participants should understand how the input they provide will be considered, the purpose of engagement and the process generally. Alternative models provide for different levels of active engagement and incorporation of suggestions. Decision-makers will need to weight the communication in the decision making balance seriously. Models of engagement can range from informing to educating, negotiating, and deliberating, etc.

Following the above review of the theoretical requirements, existing dialogues will now be surveyed. An examination of Appendix 6, which includes a list of the dialogues known to the authors, generates a series of insights that can be summarized as follows.

- Most dialogues take place in the context of research projects funded by national or supranational (e.g. EU) authorities.
- As a result, dialogues last only as long as the R&D funding. In that sense, they are not sustained dialogues. Notable exceptions include the episodic but sustained EU–US International Dialogue on Responsible Research and Development of Nanotechnology and the related, topic-based, US NSF-sponsored Meridian Institute workshops, as well as the EC-sponsored Annual Nanotechnology Safety for Success Dialogues.
- In fact, after a first wave of dialogues, the second wave seems smaller.
- Dialogues mainly involve academicians. The public authorities that fund the projects acquire most of their information through reports.

To conclude this chapter on dialogue and communication, the table in Appendix 7, lists topics and processes of dialogue between pairs of stakeholders. It highlights different communication and information needs on the part of the "emitters" and the "receivers" respectively. It also indicates the different modes (formal vs informal) of communication and their different natures (binding vs non-binding; voluntary vs mandatory).

4.4 Upstream input into research strategy and prioritization of R&D funding/risk assessment

There are many geographical levels (peer-to-peer, local, regional, national and international) and time points (technology development, market approval and post-marketng stages) at which stakeholders can engage to provide input into the data and research needed for risk assessment and its prioritization in relationship to product development. Scholars have called for upstream public engagement to involve the public in discussions about emerging technological products and research priorities well prior to market entry (Wilsdon and Willis, 2004). Upstream public engagement can be complemented by multiple other upstream endeavours, including real-time technology assessment, whereby engineers and scientists consider the social consequences of their work alongside stakeholders prior to the development of products from it (Guston and Sarewitz, 2002). In addition, upstream oversight assessment has been applied to case studies of food and agricultural nanotechnology (Kuzma *et al*., 2008). Upstream oversight assessment is a preparation tool for groups of experts and stakeholders that explores the technical features of R&D projects, examines potential risks and benefits should commercial products eventually arise from the R&D activity, and identifies data needs for addressing risks and benefits long before the product is expected to enter the marketplace (Kuzma *et al*., 2008).

Recently, environmental and consumer NGOs, academics and think tanks have raised concerns about the amount of funding that has gone to environmental and health safety (EHS) research relative to technology development. In the United States, it has been estimated that about 1 percent of the federal funds for nanotechnology are directed to EHS work (Maynard, 2006). Opening up R&D prioritization to public dialogue can help to address "public failures" of emerging technologies. Bozeman and Sarewitz (2005) argue that too much attention has been placed on avoiding "market failures" in decision-making about science and technology, and they assert that "public failures" of science and technology are equally important and can occur with or without market failures. Public engagement to develop a balanced R&D portfolio for agriculture and food nanotechnology that includes data to address uncertainties in risk assessment can not only improve risk assessment but also help to decrease the chance that public failures will occur.

It will be critical for the success of a research strategy for nanomaterials to address the key interests, priorities and concerns of stakeholders and ensure that pathways and potential risks are addressed by sponsored research. Some NGOs, among others, have discussed the importance of broad stakeholder participation in early decision-making about nanotechnology. Friends of the Earth (FoE), for example, demand public involvement in all aspects of decision-making about nanotechnology in food and agriculture, including prioritization of funding for research (FoE, 2008).

4.5 Transparency

Some sectors of the public have a relatively low level of trust in the efforts of industry and the government to assess and manage risks adequately, as evidenced by the debate on genetically modified foods. Small, unintentional actions can be misinterpreted. In particular, some stakeholders feel strongly that there should be public access to all data and that if this is not forthcoming the data are suspect, and must be a reason for non-disclosure. This can be problematic for industries, which seek to protect intellectual property, and this has been cited as a cause of the low participation with several voluntary calls for data from national and regional authorities.

The low level of trust contributes to the need for transparency in governance. A coalition of over 40 NGOs and labour organizations called recently for transparency so that the public can be made aware of the products in which nanotechnology is being used (labelling), workplace disclosure and protections, and the public release of all data used to make decisions on safety (Acción Ecológica *et al*., 2007).

Consumer confidence is currently low. Increasing transparency in governance in general and, specifically, giving the public the option to consult safety assessments would help to increase trust. Even if the public chooses not to take advantage of its oversight option, the existence of the right to do so proves reassuring. Thereby, this measure would address the consumer confidence issue directly. Fortunately, some countries offer a good example. They make all safety data available through the Internet, while protecting the confidential business information of the sponsor of the study. Such an approach qualifies as best practice.

Interest and concerns of unaffiliated public citizens

By virtue of the time and other resources that they require, stakeholder dialogues involve professionals. These professionals will act as representatives of public authorities, industries or the public. However, any comprehensive analysis must consider the interests and concerns of the unaffiliated public, a public, which, as the expression goes, “votes with their wallet”, can present a great diversity of views, and whose opinions can exhibit considerable volatility.

The interest and concerns of the unaffiliated public will bear directly on the way in which risk is socially constructed. As reminder, it is appropriate to consider not only the scientific or technological views of risk, but also the psychological and sociological perspectives, as highlighted in the FAO *Food safety risk analysis* report (Box 2.1, p. 12).

In the face of complex cognitive tasks and missing information, individuals use heuristics and other factors, such as their social and cultural influences, to make judgements about the information that they receive. As such, there is a crucial consideration for stakeholders concerned or affected by the risks with regard to how risks are presented and discussed. Public perception of hazards and risks is influenced by how they are communicated by different sources. The social amplification of risk framework (Kasperson *et al.*, 1988) explains at least partially the ways in which risks from some hazards with low probability of harm of are amplified by the ripple effect of public communications (Breakwell *et al.*, 2001; Pidgeon *et al.*, 2003). While they have been well demonstrated with a wide selection of hazards, new and emerging communication channels (e.g. blogs, Twitter, etc.) may change the nature of risk amplification.

Finucane *et al.* (2000) demonstrated that people rely on affect in judgements about risks and benefits. That is, while risks and benefits tend to be positively correlated, the perceptions of risks and benefits have a tendency towards negative correlation. In two related studies, participants were demonstrated to have relied on their affect, whether they liked a particular hazard or not, to rate the risks or benefits of items, ranging from bicycles to food preservatives. Time pressure versus non-time pressured responses both demonstrated negative correlations, with stronger responses when participants had little time for cognition, relying instead on affect. Thus, how people feel about particular technologies, beyond their knowledge, can be the basis for their perception of risks and benefits associated with hazards. The role of affect in perception suggests that research on mental models would help to frame communications. However, to date, most studies use traditional survey methods.

4.6 Consumer perception studies

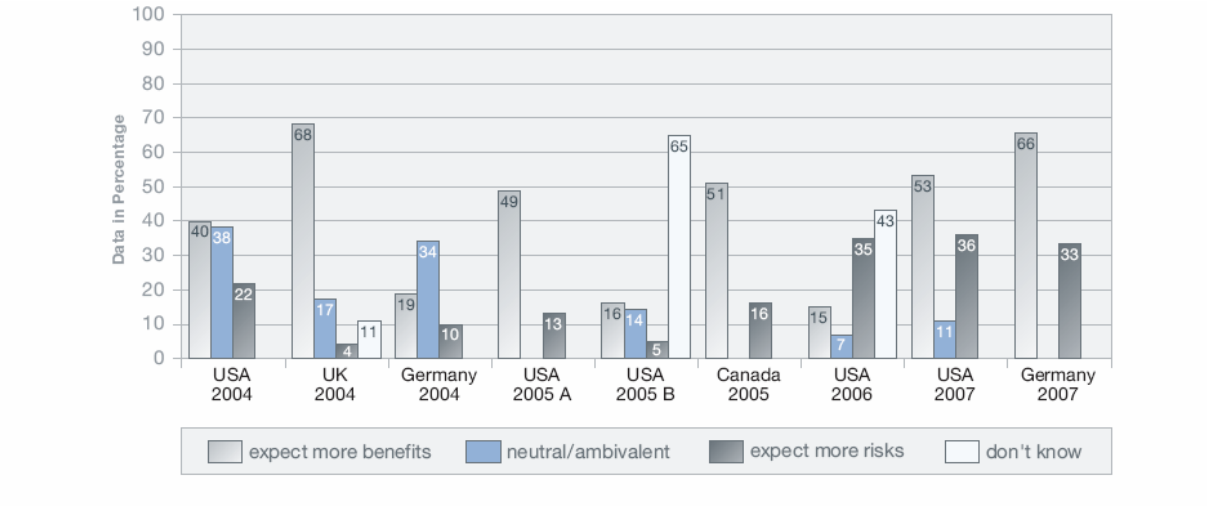
Past experience suggests that unaddressed public concerns can evolve into consumer fear of new technologies. Thus, public attitudes toward nanotechnology foods should be taken into account at an early stage of product development" (Siegrist *et al.*, 2007). An understanding of the dynamics of public perception is essential for anticipating and addressing consumer concerns regarding nanotechnology in food.

There have been several surveys of consumer perceptions of nanotechnology, and some have addressed specifically the issue of nanotechnology in food and food packaging. Most surveys were conducted in North America and Europe, and a few present cross cultural comparisons. The surveys asked whether people are familiar with the term nanotechnology, whether nanotechnology will benefit society, or whether the risks or benefits are likely to outweigh each other. Some explore attitudes towards specific applications. In general, the surveys found a relatively low level of awareness, and positive or neutral attitudes about the relative benefits and risks of nanotechnology. However, the attitudes from surveys in Europe tended to be more negative (BfR, 2006; Gavelin et al., 2007; Hanssen and van Est, 2004; Kleinmann and Powell, 2005; Nano Jury UK, 2005; Siegrist *et al.* 2007; Swiss, 2006). Grobe and colleagues describe this as a perception that any adulteration of food is "perceived as tampering with nature" (IRGC, 2008).

Several studies have surveyed initial attitudes towards nanotechnology, with some assessing changes after a definition and examples of application are given (Bainbridge 2002; Currall *et al.* 2006; Hart Research Associates 2006; 2007; Kahan 2007; 2008; Macoubrie 2005; Priest 2006). In North America a perspective among participants that the benefits of nanotechnology will outweigh the risks was found. Existing impressions of familiar technologies were found to affect perceptions of new innovations, and provision of basic information about nanotechnology greatly increases the percentage of people who see the benefits exceeding the risks. However, Kahan *et al.* (2007) observed that "people who are already predisposed to like nanotechnology (most likely because of their values or emotions) have been more inclined so far to learn about it than have those who are predisposed to dislike it". Thus public education may lead to a broader common understanding of nanotechnology applications but not necessarily to more favorable impressions.

Figure 3 summarizes the results of nine surveys that assessed consumer perceptions of the risks and benefits of nanotechnology (IRGC, 2008). They reflect generally a positive, but volatile, view of nanotechnology .There appears to be limited trust in the ability of governments or industry to address health and environmental risks adequately (IRGC, 2008).

Figure 3. Expectations of the benefits and risks of nanotechnologies



(Source: IRGC, 2008)

One caveat regarding a number of consumer attitude studies is the limitations of the Internet survey method. People recruited to Web-based surveys are more educated and more knowledgeable about science than the average person (Bainbridge, 2002). The greatest limitation of the current research is that most studies have examined only attitudes towards nanotechnology in general rather than attitudes toward potential products (Siegrist *et al.*, 2007). Only a handful of studies assessed public perception of food and agricultural applications. However, a number of researchers posed questions relevant to understanding the public attitude toward nanotechnology in food and food packaging.

The Project on Emerging Nanotechnologies in collaboration with Consumers Union, hosted a web dialogue for the public to discuss information and share thoughts about the use and potential benefits and risks of consumer products using nanomaterials (Consumers Talk Nano Dialogue, 2007). Participants felt that there were safety and ethical issues in using nanotechnology to increase food production; that food applications of nanotechnology must be well regulated and labelled; and that developing applications should proceed cautiously for now. Such studies suggest that the public wants more information about the health risks and benefits before deciding whether to purchase these products. There are also concerns about adequate oversight, unintended impacts, long-term effects and uncertain health risks (IRGC, 2008).

Kahan *et al.* (2007; 2008) conducted research into how public understanding and perceptions of nanotechnology evolve. Individuals unfamiliar with nanotechnology were found to polarize along cultural lines when exposed to the same body of balanced and accurate information, suggesting that people tend to draw conclusions from the supplied information that are consistent with their cultural bias. Siegrist *et al.* (2007) conducted a study that suggested that nanotechnology-enhanced packaging was perceived as more beneficial than other applications of nanotechnology.

Other efforts to gauge opinion in Europe have combined surveys with focus groups (Burri and Belluci, 2008; Royal Society, 2004). In general, these found that people scrutinize the potential benefits and risks in developing opinions and that they feel that nanotechnology must have tangible benefits that address societal needs. In a comparative study, Gaskell *et al.* (2005) concluded that Americans seem more optimistic about nanotechnology than Europeans, with almost half saying that such technologies will improve quality of life. Just a quarter of Europeans reported such optimism.

Research in Japan indicates a higher familiarity with and acceptance of nanotechnology generally, however this is less true for application to food and beverages (Fujita, 2006; Kishimoto 2007; 2008). Maclurcan (2008) interviewed selected individuals from Thailand and Australia. Most interviewees

thought that nanotechnology was a rebranding of earlier work in colloid chemistry, pharmaceutical research and materials science. Interviewees raised concerns that governmental policies might focus on the longer term futuristic applications rather than on near term developments.

In a general study of public perceptions on nanotechnology, Macoubrie (2005) assessed interest in the benefits of nanotechnology and found that food and agricultural application examples stimulated both positive and negative impressions. Siegrist *et al.* (2007) and Priest (2006) both observed that communicating benefit is key to gaining acceptance. Kishimoto (2007) assessed the perceived benefits and risks of nanotechnology in cosmetics, food and beverages, home appliances and drugs in Japanese subjects and found less interest in purchase of food and beverages involving nanotechnology than in other applications. Another critical theme that emerges from the existing literature is that people appear to differentiate among potential nanotechnology applications based on how and where they are used. Siegrist *et al.* (2007) confirm "that nano-inside (e.g. foods) is perceived as less acceptable than nano-outside (e.g. packaging)". In qualitative research with Swiss consumers, Burri and Bellucci (2008) heard fears that nanoparticles might cause harm to the body if integrated into food. The Royal Society study (2004) found that: "[A]pplications that remained on the surface of the body, such as sunscreens, were not felt to carry the same level of risk, although respondents still expressed concern about them".

Consumer attitudes towards applications of nanotechnology in food and agriculture sectors are complex. Consumers want to understand the potential risks and benefits of nanotechnology and they want tangible benefits to be clear. Without obvious benefits, consumers are unlikely to have positive impressions towards, much less a willingness to buy, nanotechnology-enhanced food products. Even if the perceived risks are low, consumers may still not want to purchase nanotechnology-enhanced food products.

4.7 Stakeholder organizations

As stated in the introduction, stakeholders are broadly defined to include organizations and individuals that are affected by the introduction of nanotechnology and nanoscale materials into the food and agriculture sectors. Effective engagement must identify correctly and engage these stakeholders, or excluded parties may threaten the process. Categories of stakeholders include individual citizens and members of the public, who will become decision-makers about the adoption and incorporation of these materials and processes into the food supply. Organizational stakeholders include several types of advocacy organizations, including environmental and consumer advocates, scientific, think tank, and science policy groups, industrial advocacy and trade organizations, and the labour force. Governmental organizations also represent important stakeholders, because the decisions of one entity may affect many others at the international, national, regional and local levels.

Environmental and consumer NGOs

A recent report highlighted the diversity of environmental NGOs in their level and types of engagement, explaining the differences as "shades of green" (Hoffman, 2009). There are many shades of NGO participants in the nanotechnology arena. Activities include protests, government petitions, detailed reports, public demands, participation in public meetings and hearings, and industry partnerships. Some employ scientists and produce reports using science-based arguments to make the case for the environmental health and safety, and the ethical and societal concerns expressed. Advocacy organizations are important stakeholders because they represent consumer, labour, environmental, agricultural, biological and other interests, and many are well funded, building on new and prior collaborations, and can make arguments similar to those made about genetically modified foods. Advocacy organizations are often viewed by the public as trustworthy sources of information. Below is a chronology of recent activities and reports by international advocacy organizations.

Table 4. Partial list of advocacy reports and activities

ETC Group	*Down on the farm: the impact of nano-scale technologies on food and agriculture* (2004)
International Center for Technology Assessment (ICTA), Friends of the Earth (FoE) and coalition of groups	Citizens' petition to the FDA on sunscreens (May 2006)
45 NGO – coalition International	*Joint statement of principles for the oversight of nanotechnologies and nanomaterials* (2007)
Environmental Defense Fund and DuPont	*Nano risk framework* (July 2007)
Natural Resources Defense Council (NRDC)	*EHS nanotechnology framework* (May 2007)
The Soil Association (UK)	Ban on nanomaterials from the organic cosmetics, foods and textiles that it certifies (Jan 2008)
Friends of the Earth (FoE) Australia	*Out of the laboratory and on to our plates: Nanotechnology in food and agriculture* (March 2008)
ICTA-led coalition	Sues US EPA for failure to regulate nanosilver (May 2008)

There are commonalities and diversity among the issues raised by these and other advocacy organizations. Common issues raised by NGOs (Lee, 2006; Parr, 2006; Wilsdon, 2006) in relation to nanotechnology in food and food related applications include:

Safety:

- a need for further safety testing and regulatory oversight of the development, testing and application of nanomaterials;
- consideration of the societal impacts of nanotechnology beyond the narrow definition of safety normally applied;
- A precautionary approach where safety data are inadequate.

Transparency:

- Labelling of foods and food products to ensure that consumers are aware of the presence of nanomaterials;
- Public availability of safety testing data to support informed choice;
- Public visibility of nanotechnology development.

Engagement:

- Opportunities for meaningful engagement of the public and NGOs in decisions concerning nanotechnology;
- Equity of access to and impact of nanotechnologies.

Other suggestions include increased international cooperation in the development and regulation of nanotechnology; the regulation of new technologies by a United Nations body; a reform of the intellectual property regime governing nanotechnology; a moratorium on the sale of products containing nanomaterials, particularly those in food; the development of equipment to detect nanoparticles.

Analysis of the key issues

The most prominent voices commenting on nanotechnology as it applies to food and agriculture are environmental groups, particularly those that deal primarily with genetic modifications and organic farming (bio-oriented advocacy NGOs), alongside those who advocate on a range of environmental topics (global-oriented environmental advocacy NGOs). Both have been able to build strong constituencies over time. Environmental NGOs that concentrate on toxicology issues (toxics-oriented advocacy NGOs) form a slightly less significant group, but are still relatively strongly represented considering their lower absolute numbers. The strong representation of organizations that deal with the ethical application of science and technology is also noteworthy (O'Neil and Ackland, 2006).

A major portion of the outcry against nanotechnology results from the continuing promotion of new applications despite critical uncertainties about the extent or severity of various impacts. It is unclear what proportion of NGOs might change their positions on nanotechnology if substantial new scientific information became available. In the meantime, many NGOs will still advocate for a moratorium. It is clear that what labour, environmental and consumer advocacy groups all share is a desire to have sufficient time to determine the risks before widespread effects are seen.

It is possible to identify trends in the demands of NGOs according to their advocacy area. For example, the most common demand from consumer groups is an open public dialogue on nanotechnology, followed by calls for regulation and increased testing. (Interestingly, a moratorium is not included in these demands). Calls from environmental (bio-oriented) groups most often concern a moratorium, followed by regulation and labelling – in effect, putting the most precautionary option first, and moving downwards in levels of consumer protection, creating a logical flow of events to protect humans. Environmental (globally-oriented) NGOs are most likely to demand regulation, public dialogue and increased research on nanotechnology. Groups promoting ethical science and technology cite regulation and a moratorium most often; however they have also put forth a variety of other suggestions.

The common denominator across nearly all advocacy NGOs appears to be that discussion is needed to determine the necessity of policy interventions on the introduction of nano-engineered particles and processes into commercial products as long as the potential safety threats cannot be adequately measured and evaluated. Nearly all expressed a desire for industry and governments to implement measures of some kind to protect the health and safety of workers and the public from the consequences of the unregulated release of commercial nanoproducts into the environment.

Industries

Industry NGOs, or "trade associations" as they are more commonly referred to, often serve as the interlocutor in dialogues between public authorities and industry, or between consumer organizations, environmental NGOs and industry. They offer a single contact point, provide position statements representing the industries' views – in particular on existing and proposed regulation – can serve as think tanks or coordinators of projects that industries could not undertake in isolation, including responding to calls for voluntary information, and, more generally, provide a means for industry to express itself without putting the image of a given company at risk. In the context of food, examples of such trade associations include CIAA, the European Food and Beverages Industries Association in the EU, the Groceries Manufacturers Association in the United States, AFGC in Australia, and the Japan Food Industry Center.

Governments

Government is viewed as an important stakeholder in this context. Government has ultimate responsibility to protectthe safety and well-being of consumers, the environment, and other common interests of the public. Government also plays a critical role in envisioning and leading the advancement of science and technology to sustain economic development and resource management. Hence, it must support and monitor responsible development and the deployment of new technologies.

It should be recognized that different parts of government, such as legislative and executive branches, have different roles. The principle of check-and-balance is in place to ensure that the interests and concerns of all other stakeholders are heard and considered in developing and implementing policies. Also, different levels of government, namely national, provincial and local, also have their responsibilities to their constituents, including private citizens, as well as to economic development in their respective areas. Furthermore, international governmental organizations such as FAO, OECD[10] and WHO, and supranational governmental entities such as the EU have used their respective resources and instruments to protect the interests of their member countries. It is vitally important to call for effective coordination and cooperation to allow communication of benefits and risks among these government entities, so as to encourage and support sound policies and practices to govern the advancement of nanotechnology for agriculture and food while ensuring safe use of the new technologies.

A number of studies have assessed the relevance and adequacy of existing regulatory frameworks to identify any potential inadequacies and gaps in relation to the potential risks arising from the use of nanotechnologies in food and agriculture sectors.

In many cases, pre-market evaluation of food products is likely to be relevant to nanotechnology applications. Examples include horizontal legislation, such as general food safety laws and chemical safety laws. Other vertical regulations also exist, such as those regarding food additives, novel foods, specific health claims, FCM, water quality, and other specific regulations relating the use of certain chemicals, such as biocides, pesticides, veterinary medicines, etc. Other environmental regulations may also capture the unintentional or accidental presence of engineered nanomaterials in agrifood products. Similar instruments exist within the Codex Alimentarius, e.g. codes of hygienic practices, food additive provisions, MRLs for pesticides and veterinary drugs, health claims, guidelines, etc.

The outcomes of the joint FAO/WHO Experts Meeting on the applications of nanotechnologies in food and agriculture sectors could be used to identify any need for specific regulatory provisions in the Codex Alimentarius.

Science, science policy, think tanks, and professional organizations

This group of stakeholders includes organizations that have significant independence and technical expertise in fields related to science and technology. Many of these bodies draw upon the advice of expert committees and could provide a forum where citizens and stakeholders are included in two-way communication in the presence of experts about the risks and benefits surrounding agriculture and food nanotechnology.

The Royal Society in the United Kingdom and the United States National Academies have taken prominent roles in analysis of the funding and policy issues surrounding nanotechnology (NRC 2006; 2008; Royal Society, 2004). Other academies of science around the world, such as the Third World Academy of Sciences, could be a valuable source of risk information and support dialogue in developing countries.

Science museums are another venue for connecting experts with stakeholders and the public. In the United States, the Nanoscale Informal Science Education Network (NISEnet), a network of several science museums across the country, has engaged citizens in public fora. These events have included discussions about the applications, potential risks and benefits surrounding nanotechnology, and values and decision-making about nanotechnology products (NISEnet, 2009).

Think tanks and professional organizations also have key roles to play. The Society for Risk Analysis, an international society, convened a special meeting on risk analysis for nanotechnology in 2008 and continues to support dialogue about methods and data needs for risk assessment. Think tanks can be a

[10] OECD's Programme on the Safety of Manufactured Nanomaterials: http://www.oecd.org/env/nanosafety/
OECD's Programme on Science and Technology Policy on Nanotechnology: http://www.oecd.org/sti/nano

key source of risk information and provide independent ground for public dialogue. The Foresight Institute, Project on Emerging Nanotechnologies (United States), Nanotechnology Think Tank (the Netherlands), the Innovation Society (Switzerland), International Risk Governance Council, and Meridian Institute are examples of active organizations that have provided reports and dialogues related to risk issues surrounding ENMs.

In summary, this group of stakeholders has not only an important participatory role to play, but also responsibilities to convene and provide balanced information on risks, benefits and societal values surrounding ENMs.

4.8 Relevant theories of risk perception

There are several theories about the way people perceive risks and hazards, and these are informative for considering communication models for risk assessment of nanotechnology and nanomaterials in food and agriculture. The table below, and the subsections that follow, represent a few of the widely discussed theories, which seek to explain the reasons that some types of hazards raise higher levels of concern among stakeholders than scientists or decision-makers would anticipate based on probabilities. This section is not comprehensive. It may prove useful to explore in greater depth how theories of risk perception can inform effective stakeholder dialogues about emerging technologies.

Table 5. Theories of hazard/risk perception

Theory	Brief summary
Cultural theory	People respond to risk messages according to their cultural affiliation.
Mental models	People develop perceptions of risk based on the associations they make with other types of risks.
Social amplification of risk	Public perception of risk can be influenced by the number and type of messages received.
Psychometric paradigm	A general set of psychological factors can be predictive for how technologies will be perceived.

Cultural Theory

Different groups of stakeholders play different roles in any dialogue. This proves even more true as concern centres on a technology or a set of technologies like nanotechnologies. Indeed, as already pointed out, the views of different groups will vary greatly, not only regarding the assessment of risks and benefits but also in terms of their respective contributions to the exchange.

The "Cultural Theory (CT)" developed by British anthropologist Mary Douglas and co-workers (in particular, Douglas, 1992; 1996; Douglas and Wildavsky, 1982; Gyawali, 2001; Thompson *et al.*, 1990) provides useful insights into the likely expectations, positions and behaviours of different groups of political actors. Historically, CT used nuclear power as its first test case. It places its emphasis on social organization rather than on economic or cognitive factors. Thereby, CT offers a different, complementary angle on stakeholder roles. This also means that the present section gives a perspective different from the previous ones because it focuses more on social aspects than cognition. Cultural Theory identifies five solidarities, namely: "Hierarchy", "Individualism" , "Egalitarianism", "Fatalism", and "Withdrawal". We shall consider only the first four, "involved" solidarities.

In a hierarchy, individuals belong to a group, and their rank, status or station determines their behaviour. With individualism, individuals stay isolated and enjoy freedom. Egalitarianism establishes a clear distinction between those who belong to the group and those who don't, while taking care of equality among members of the group. Fatalism regroups compliant and un-organized individuals. Table 6 summarizes some of the characteristic traits of the four involved solidarities. It also allows a

check of the appropriateness of mapping "Public Authorities", "Industry" and "NGOs" onto "Hierarchy", "Individualism" and "Egalitarianism."

These different groups have different perceptions of risk and different attitudes towards it. Hierarchs will manage risk as a problem with a solution. Individualists will take the risk; they will try to use it, seeing it as an opportunity. Egalitarians will consider risk an economic "bad". More often than not, they will limit the risk assessment to a hazard assessment. They will seek to avoid the risk at almost any cost. Lastly, Fatalists will accept the risk and bear with it. These fundamentally different attitudes will determine both the nature and the content of contributions to a dialogue.

Fatalists will prove virtually impossible to engage. The three other active solidarities will respectively make contributions pertaining to: (i) procedures (Hierarchs), (ii) substance (Individualists), and (iii) principles and, by means of the Absolute colliding with the Relative, problems, issues, and shortcomings (Egalitarians). This means that the three engaged solidarities will never agree completely either on what to talk about, what to do about it or how to do it. Compromises, i.e. imperfect resolutions, constitute the only options. While less "pleasing to the eye", such clumsy compromises offer the promise of solutions that qualify as more stable (a hierarchical concern), more productive (an individualistic interest), and more in line with established scientific and democratic principles (in particular, equity) (an egalitarian preoccupation) than those arrived at by one solidarity or as a result of an alliance between two solidarities. Therefore, involving all solidarities in stakeholder dialogues – which, in practice, means engaging "Public Authorities", "Industry" and "NGOs" as well as members of the public who are not organized – serves the interest of reaching democratically legitimate, operationally useful and socially acceptable outcomes.

Table 6. Cultural theory solidarities

	Hierarchy	**Individualism**	**Egalitarianism**	**Fatalism**
Individuals that subscribe to it…	belong to a social group and their social position dictates their behaviour	do not belong to a social group and their social position does not dictate their behaviour	belong to a social group and their social position does not dictate their behaviour	do not belong to a social group and their social position does not dictatestheir behaviour
Example no. 1	administration	entrepreneur	NGO	victims
Example no. 2	wolves	hawks	vultures	donkeys
Risk is to be…	managed	taken	avoided	accepted
Actions concern…	procedures, regulation	innovation	precaution	nothing, until riots break out
Communication focuses on…	doctrine, measures	features, prospects	principles, problems	(not applicable)
Risk assessment focuses on …	hazard and exposure	exposure	hazard	hazard
Response to missing information	ranges from "more research is needed" to "moratorium"	"innocent until proven guilty"	"dangerous unless proven innocuous"	"no news is bad news"
Response to additional information	reassurance	reassurance	alarm	alarm

(Source: Elaborated on the basis of a presentation by Philippe Martin at the ECETOC meeting of 9 November 2005 in Barcelona, Spain)

Psychometric paradigm

The psychometric paradigm is based on studies to explore what features of technologies and their associated products contribute to risk perception. The paradigm is empirically driven, with theories arising from analyses of observations and experiments. Early iterations of the paradigm suggested that perceived risk was largely determined by two factors: novelty and dread (Fischhoff *et al*., 1978). Novelty includes subfactors such as whether the effects of the technological hazard are known or unknown, observable or unobservable, immediate or delayed, and old or new. Dread includes subfactors such as whether the effects are controllable or uncontrollable, fatal or non-fatal, equitable or inequitable, voluntary or involuntary, and future or present (Slovic *et al*., 1985).

Since the publication of the original paradigm, emotional responses and trust have also been added to the model of important factors in risk perception. Trust in the actors involved in risk analysis and management has been shown to influence risk perception (Slovic *et al.*, 1991). Studies have also shown a correlation between feelings or attitudes towards the subject of risk and risk perception ("affect heuristic") (Finucane *et al*., 2000).

Much of subsequent research in risk perception has been informed by the psychometric paradigm, although there have been studies that point out its shortcomings in excluding other variables such as mortality, cultural attitudes (see Cultural Theory section), economics, and views about "tampering with nature" (Sjoberg, 2006). Regardless, the paradigm or a more inclusive version of it could help guide public engagement towards ENMs in agriculture and food and their potential risks and benefits. Initial questions to guide engagement activities could highlight controllability, uncertainty, feelings, trust, novelty, mortality, economic consequences and equitable distribution of risk. Stakeholders would be open to discuss whether or how these factors matter to them in the context of a specific ENM in food or agriculture.

Social amplification of risk

The social amplification of risk framework (Kasperson *et al*., 1988), explains at least partially the ways that risks from some hazards with low probability of harm are amplified by the ripple effect of public communications (Breakwell *et al.*, 2001; Pidgeon *et al*., 2003). The media, or other sources of information, play a role in perceptions of the level of risk, and can raise the level of concern by overplaying the risks through a focus on hazard or uncertainty.

The social amplification of risk theory links the communication of messages about a risk event with the public perception of the hazard. The way in which the messages are explained can influence the significance of the event in the receiver's view, which can distort the messages and affect responses to them, in some cases amplifying their relative importance. The amplification can cause a ripple effect, with broader social and economic impacts resulting from it.

A critical review of the social amplification of risk framework (Breakwell and Barnett, 2001) found limitations in its ability to capture the complexity of drivers of risk perception; however, note that "the nature of risk amplification is affected by the ways in which regulatory agencies respond to the concerns of interested publics and stakeholders. In fact, unnecessary intensification may be averted by timely action by appropriate agencies". These authors suggest that implications for government organizations include:

- they should examine how they perform in controversies;
- they should analyse how they interact with the media in controversies;
- develop a policy for media briefing during the life cycle of the controversy.

While well demonstrated for a breadth of hazards, new and emerging communication channels (e.g. blogs, Twitter, etc.) may change the nature of risk amplification.

4.9 Good communication

Effective communication and dialogue among all stakeholders

Evaluating the effectiveness of communication and dialogue requires evaluation criteria. Communication and dialogue will share some of the criteria, but some will differ.

Communication and dialogue should inform the democratic decision-making processes, now often dubbed, especially in Europe, "governance". This democratic imperative sets as a minimal requirement that communication and dialogue base themselves on factual information translated in terms understandable to the audience or the stakeholders: (i) from independent sources – or, short of that, from sources whose interests are declared and do not pose a problem, (ii) of the best quality possible, and (iii) obtained in a transparent manner that peers can verify, could replicate, and have actually validated and/or reviewed. In addition, the process governing the communication and dialogue should meet criteria of openness and clarity of purpose in order to ensure trust and reasonable expectations.

In addition to what could be referred to as "democratic" criteria, effective communication requires taking cognition and affect (or cultural affiliations) into account. In practice, talking about the risk of something that people do not know about or for which they cannot assess the benefits will result in the attribution of a high level of risk. This is exacerbated when compounded with the documented limits of reasoning, by laypeople and experts alike, about risk and probability (see for example Gigerenzer, 2003). Moreover, affect and social affiliations will play an essential role that often proves difficult to decode. Indeed, what sometimes appears as public hysteria frequently emerges from a complex competition between the four competing cultural visions identified by Cultural Theory within an individual and between individuals. While recommending adherence to a strict code of ethics verified by ethical boards, we have to ask whether communication on risk with non-experts might work better by putting things in context, i.e. by including benefits. One might also wish to issue a recommendation that is impossible to satisfy; namely, an "affect-neutral" form of communication. Given that our thinking processes and the physiological machinery that sustains them evolved on the basis of concrete objects, it is simply not possible to speak a metaphor-free – and, therefore, an affect-free – language. Nevertheless, we can aspire to linguistic formulations that respect and cater to the interests of each one of the Cultural Theory solidarities and, thereby, delay the adoption of a position through cultural affiliation.

The experimental investigation by Kahan *et al*. (2007, p.31) provides the basis for this proposal. The study indicates that, as members of the public learn more about nanotechnology, their assessments of its risk and benefits diverge, contrary to what one would expect. Specifically, those "who hold values that predispose them to credit claims of environmental risk generally tend to become alarmed, whereas those who hold values that predispose them to dismiss claims of environmental risk generally tend to be become reassured." This led Kahan *et al*. to formulate what they consider the major conclusion of their study: that "mere dissemination of scientifically sound information is not by itself sufficient to overcome the divisive tendencies of cultural cognition". Those in a position to educate the public – from government officials, to scientists, to members of industry – must also frame that information intelligently in ways that make it possible for persons of diverse cultural orientations to reconcile it with their values.

In summary, effective communication and dialogue necessitates respect for democratic and ethical criteria as well as taking into account how individuals think and react to information. Again, we find ourselves in the realm of the imperfect because these different imperatives place antagonistic demands on communication and dialogue. Effective communication and dialogue will need to balance these different elements on a case-by-case basis with past experience as moderately reliable guides, with respect as a prerequisite, and listening as an absolute requirement.

Effective dialogue with the media

The problem with all types of scientific controversy, whether it be nanotechnology, genetically modified organisms, the measles, mumps, rubella (MMR) vaccine, animal experimentation or climate change, is that the immediate void created following a breaking news story is usually filled by individuals and organizations with a specific agenda and a sophisticated understanding of how to take advantage of media opportunities. Such groups and individuals recognize that each news wave provides them with a chance to get their voice heard.

The imbalance comes when scientists, doctors and engineers are not part of this mix. Most experts will either not be in a position to correct misinformation and inaccuracies, owing to institutional restrictions on their independent engagement with the media, or be disinclined to seek media attention by doing so. Even where an expert has the inclination and authority to correct the public record or contribute to a public debate, most lack appropriate avenues into the news media. In this respect many experts are comparatively disadvantaged in terms of access to the media. The tight time dependence of media interest and potential criticism by colleagues who may disapprove of seeking media limelight may further inhibit willingness to approach the media.

As a response to these difficulties and inhibiting factors, the concept of a Science Media Centre (SMC) was developed. The first was set up in London in 2002 with others established in Australia in 2005, New Zealand in 2008 and Canada in 2009. The Centres work to get evidence-based science and credible scientists into the news media, at the time when society needs them most. Commentary must be independent, news-wise and free of any agenda other than the promotion of good evidence-based science for the good of society. By monitoring news and looking for opportunities to feed science into headline news, the SMCs are perfectly placed to help the scientific community handle controversy. This way of working is not without its challenges. Scientists find the timeframe of news hard to handle. They want time to review all the facts and consider all the issues before commenting on breaking stories. As a matter of professional ethics they are generally unwilling to speculate beyond a reasonable extrapolation of existing data and yet speculation is essential in the fast-paced game of the news cycle. By the time they feel comfortable, the opportunity may well have passed.

Speed is critical. Reaction from experts must be fast, credible and focused on evidence. Reaction can also be staggered – with large controversial stories there is more than one opening. An opportunity may arise to present high level concepts where confidence in the reliability of the facts is high, with the admission that some facts are unknown at that early stage of the debate or issue. As more information is obtained and assimilated more definitive statements can be made.

Publicly controversial studies are not published by their authors to mislead the public wilfully, but rather their message, once translated into press releases and news stories, loses its qualifiers and context. Most scientific publications explore various interpretations of the research results, or postulate an explanation as a basis for further research rather than a firm conclusion. Usually, however, only one interpretation is communicated to the public. By providing independent and nuanced comment on these stories, scientists help fill this gap and offer the public help in interpreting the information.

There is a view that scientists should reach consensus over controversial issues before airing them in public. However, not only is it impractical to keep new research from the media, such control assumes that people can only take on board a limited amount of information and cannot make up their own minds on the basis of a mix of viewpoints. Such an approach also has the potential to undermine public trust in science. A coordinated media approach on controversial issues fuels conspiracy theorists who believe that scientists are simply out to further their own research careers or, worse, that they are working to a hidden government or industry agenda. Of course individual experts can and do have agendas and opinions that are not necessarily founded in hard evidence. Thus an evidence-based discussion is critical to supporting informed debate in the community.

The public often do not understand, or forget, that the research community is not a cohesive group with a single message. Scientific research is highly competitive and iterative, which helps to keep the

evidence at the fore: for every claim not supported by the evidence, there is a scientist to point this out with references and citations to support healthy scientific debate. Unfortunately this tends to happens out of public view, in conference rooms and scientific publications where the language is not accessible to most of the public.

Greater access of scientists to the public debate where their evidence and expert arguments can be shared would support informed public debate and assist the public in forming their own conclusions having heard a rich mix of competent voices.

4.10 Summary and conclusions

Development of transparent and constructive dialogues among stakeholders entails many aspects. Different readers with different cognitive inclinations, appreciations of risk, stakeholder group affiliations, etc. would certainly gain different insights from this chapter.
The "provocations" that we would like to submit include the following messages:

- Food is a sensitive issue, one of the most sensitive in the nanoscience/nanotechnologies area. Nanofood may prove too hot to handle for those who pay lip service to the public and who ignore or fail to grasp the subtleties of communicating with and engaging citizens.
- Public engagement acquires meaning only if focusing on issues that have real significance to the participants from the public. Issues that the public deems important concern safety, benefits to citizens, language/terminology, R&D funding priorities, and regulations and their implementation. If it fails to address topics close to the hearts of citizens and result in concrete outcomes, public engagement leads to frustration, mistrust and, ultimately, public opposition.
- Engagement may in the longer term require institutional, if not regulatory, adjustments because of the de facto superposition of different streams of democratic dialogue, formal and informal ballots, and decision-making processes.
- Public engagement entails the basic requirement of agreeing on a common parlance.
- With respect to public interests, perceptions and concerns, no amount of intellectual power will ever replace well-designed polls, surveys or engagement activities. Moreover, public interest, perceptions, and concerns change with the culture, even the culture within a stakeholder group, and over time.
- Beyond cultural considerations, government authorities universally can foster greater public confidence through institutional efforts to provide thorough oversight of applications of nanotechnology in food and packaging that are transparent and allow public involvement.
- Public (real) knowledge of nanoscience and nanotechnology applications is growing exponentially, worldwide, and this may affect the delicate balance of benefit to risk perceptions.
- In addition to "benefits" as a key factor both in terms of risk-rating and consumer willingness to buy, "use" and, implicitly or explicitly, exposure stand out as determinants.
- Promotion of new applications without having the capacity to demonstrate their safety stands out as a very efficient generator of outcry, a sure recipe for commercial disaster. Corporations will benefit from integrating this empirical observation into their strategic thinking process.
- A first wave of dialogue has found its conclusion. The second one is smaller. Will it meet the call for more open public debates, in particular on the nature and degree of public/regulatory intervention needed, issued by environmental NGOs and consumer organizations?
- Cultural considerations suggest that no uniform solution exists for transparent and effective communication and dialogue. Nonetheless, we can find suitable pragmatic arrangements that take into account the level of knowledge of the interlocutor, cognitive processes, risk aversion and cultural affiliations, as well as scientific and democratic principles.
- Involving all stakeholders in dialogues – which, in practice, means engaging "Public Authorities", "Industry" and "NGOs", as well as members of the public who are not organized – serves best the interest of reaching democratically legitimate, operationally useful and socially acceptable outcomes.

- Considerations of cultural cognition also provide a robust working hypothesis for when some stakeholders have an opinion about something that they know nothing about. Indeed, the latest research in this area suggests that the cultural affiliation will tend to dictate the position adopted, rather than some rational or irrational weighting.
- Effective communication and dialogue necessitates respect for democratic and ethical criteria as well as taking into account how individuals think and react to information. These different imperatives place antagonistic demands on communication and dialogue. Effective communication and dialogue will need to balance these different elements on a case-by-case basis.
- With respect to effective dialogue with media, allowing the public to form their views on the basis of a "rich mix of competent voices" – and giving scientists the freedom to go to the media – would serve the interests of democracy best.

As provocations, the messages issued in this conclusion should be taken with a grain of salt. They merely attempt to go beyond "good old common sense." In truth, they seek to break a pattern. These invitations to think a bit differently aim at avoiding repeating well-documented, past mistakes and making nanoscience and the nanotechnologies not only scientific and commercial successes but also democratic achievements.

5 Recommendations

5.1 Nanotechnology applications

Consideration should be given to provision of an authoritative database that keeps track of the current and emerging materials, products and applications of nanotechnologies in agri-food sectors.

- There are a number of different definitions relating to processes, materials, products and applications of nanotechnologies. There is a need for agreement on a specific set of clear and internationally harmonized definitions that relate to the agrifood sector, and FAO/WHO should support activities in this direction.
- There is a need to develop a procedure for classifying nanostructures in agrifood products that supports risk governance for ENMs.
- The outcomes of this meeting should be used to provide a basis to identify the need for possible analysis of gaps to ensure that applications of ENMs in the agrifood sector are covered adequately under the provisions within the Codex Alimentarius.
- There is a need to consider the whole life cycle of ENMs in agrifood applications.
- Because of potential public health implications, the use of biopersistent ENMs in the agricultural sector, which may persist or accumulate in the body or the environment, should be considered in terms of the subsequent exposure during production and use, and through possible contamination of agrifood produce, soil, water, etc.

5.2 Risk assessment

The current risk assessment approach used by FAO/WHO and Codex is suitable for ENMs in food and agriculture, including the effects of ENM on animal health.

- FAO/WHO should continue to review its risk assessment approaches, in particular through the use of tiered approaches, in order to address the specific emerging issues associated with the application of nanotechnologies in food and feed.
- FAO/WHO should consider seeking further scientific advice on the use of a tiered risk assessment approach for application of nanotechnologies to food and feed. This should consist of an initial screening level, to characterize the material, and to estimate toxicity and exposure or dose–response relationships. This is followed by progress through more refined and data-intensive tiers if appropriate. Implementation of this type of approach will result in increased knowledge of the relationships between physicochemical characteristics and biological interactions. Ultimately this may enable the prioritization of types or classes of materials where additional data are likely to be necessary to reduce uncertainties in the risk assessment.
- In support of this tiered approach FAO/WHO is recommended to develop a decision tool to support identification of the appropriate risk assessment approach to categories of nanomaterials.
- This expert meeting recommends FAO/WHO to encourage the innovative and interdisciplinary research that may lead to novel risk assessment strategies for the application of nanotechnologies in food and feed, while maintaining or improving the current level of protection.
- The use of innovative approaches can at the same time lead to reduction, replacement or refinement of animal experiments, for example by the development of tiered approaches that rely heavily on alternative approaches to testing.
- The development of validated testing methods and guidance would address data gaps in the following areas:
    - physical and chemical characterization methods appropriate for ENMs in food and feed matrices during the product life cycle, taking into account dynamic processes related to these parameters in various matrices;
    - characterization of ENMs in food, feed and agricultural matrices;
    - determination of the presence of NP in biological tissues;
    - *in vitro*, *in vivo*, *ex vivo* and *in silico* assays for assessment of potential toxicological effects of ENM;

    - biokinetic properties of ENMs, specifically because of the potential of ENMs to pass biological barriers (mucosa, blood–brain barrier, blood–milk barrier), novel distribution patterns, and mechanisms of metabolism and excretion. It is further recommended to correlate these data with physicochemical characteristics;
    - characterization of ENMs using dose metrics other than mass concentration.
- International organizations (FAO/WHO) should consider requesting, collating and disseminating the following types of data:
    - background levels of ENM in food and feed matrices;
    - amount and form of ENMs in food and feed commodities resulting from the use of NM applications in the food and agriculture sectors;
- The expert meeting recommends FAO/WHO to stimulate the utilization of knowledge from other sources in the risk assessments, whilst recognizing that this is a major undertaking.
- Sources could be epidemiological studies or clinical studies (pharmaceutical, material sciences, etc.).

5.3 Stakeholder confidence

FAO/WHO should provide a forum for continued international dialogue to develop strategies to address stakeholder issues surrounding the development of nanotechnologies in food, water and agriculture.

To help address "public failures" of emerging technologies, FAO/WHO should consider launching a participatory engagement effort on agriculture and food nanotechnologies with a broad range of stakeholders, including public authorities, industries, environmental NGOs, consumer organizations, scientific organizations, professional communicators and members of the general public. The purpose is, in particular but not exclusively, to raise awareness among: (i) policy-makers – regarding the importance of engaging the public while taking into account the various facets of risk (scientific and technical, cognitive, psychological and sociological) and their implications for risk assessment, communication and management; (ii) analysts – concerning the value of evaluating the outcomes of past dialogues and relaying these findings to policy-makers and other stakeholders in agriculture and food nanotechnology systems; (iii) R&D funding agencies – with regard to opening up R&D prioritization to public dialogue; (iv) all stakeholders – with respect to increasing understanding of the interests, concerns and positions of one another. Further, such an international dialogue can serve as a non-binding venue to identify emerging issues for later consideration by international, multinational and national organizations (see recommendation below).

FAO/WHO should encourage Member Countries to engage the public on applications of nanoscience and the nanotechnologies in food and agriculture. In support of this engagement, FAO/WHO should provide guidance, training and capacity building resources for governments to engage stakeholders.

- The dialogue should focus on issues that the public considers meaningful in a proactive and responsive way, lead to identifiable outcomes, and include an ex-post evaluation of the engagement activities. FAO/WHO is invited to make the best use of the outputs of the FAO/WHO public engagement process, existing information resources on consumer perception and public attitudes, and the evaluation of the outcomes of existing stakeholder dialogues on nanotechnology.
- Issues that the public considers meaningful include, but are not limited to, safety, benefits to citizens, language and terminology, R&D funding priorities, regulation and its implementation, and congruence with social and cultural values. While not an exhaustive list, prerequisites for good dialogue include: (i) having a clear purpose, (ii) communicating this purpose to participants, (iii) sharing a common language, (iv) addressing issues raised in consumer perception surveys and previous public engagement exercises, (v) ensuring adequate time is available, (vi) taking cultural aspects into account, (vii) making the dialogue open, transparent and representative, (viii) ensuring that participants trust the host, that a

trusted facilitator manages the process, and that participants have access to trusted information sources and trusted experts, and (ix) upholding established scientific and ethical principles.

- Key issues that emerge for consideration in any communication include risks, benefits, use, evidence, exposure, social values, economic impacts, affect and trust. In this context, science communication and education contribute directly to the quality and usefulness of dialogues. Therefore, scientists and science communicators have a crucial role to play. Scientists will also make a decisive contribution in developing high-quality, independent and balanced information on the risks and benefits of the applications of nanoscience and the nanotechnologies in a transparent manner. Communication should take advantage of different types of media (for example, printed press, press releases on published studies, radio, TV, Internet, public speeches, etc.).
- FAO/WHO should review the existing FAO/WHO food safety risk analysis framework in light of other analytical deliberative frameworks, in particular with regard to engaging stakeholders.
- In recognition of the importance for trust building, FAO/WHO should identify mechanisms to support the need for transparency and traceability of nano-enabled products or ENMs in food and agriculture and their associated risks.
- Given the international role of FAO/WHO and considering the multitude of cultural contexts, FAO/WHO should take the lead in developing an evaluation process to assess the success and value of public engagement strategies for nanotechnology applied to food and agriculture.
- This Expert Meeting recommends FAO/WHO to strengthen communication and cooperation with other intergovernmental organizations, such as those of the IOMC, in order to ensure complementarily in their respective activities, while avoiding duplication of work.

6 References

Acción Ecológica 2007. Principles for nanotechnologies and nanomaterials oversight. http://www.iufdocuments.org/www/documents/Principles%20for%20the%20Oversight%20of%20Nanotechnologies%20and%20Nanomaterials.pdf

Aitken, R.J., Chaudhry, M.Q., Boxall, A.B.A. & Hull, M. 2006. In-depth review: Manufacture and use of nanomaterials: current status in the UK and global trends. *Occupational Med. – Oxford,* 56: 300–306.

Akbari, Z., Ghomashchi, T. & Moghadam, S. 2007. Improvement in food packaging industry with biobased nanocomposites. *Int. J. Food Engineer.* [online], 3(4): article 3, 24 August 2007. www.bepress.com/ijfe/vol3/iss4/art3. ISSN 1556-3758.

Alkhamis, K.A., Salem, M.S. & Khanfar, M.S. 2009. Determination of the mechanism of uptake of organic vapors by chitosan. *Pharm. Dev. Technol.*, 14(1): 90–95.

Araujo, L., Löbenberg, R. & Kreuter, J. 1999. Influence of the surfactant concentration on the body distribution of nanoparticles. *J. Drug Target.*, 6(5): 373-385.

Back, E.I., Frindt, C., Oćenásková, E., Nohr, D., Stern, M. & Biesalski, H.K. 2006. Can changes in hydrophobicity increase the bioavailability of alpha-tocopherol? *Eur. J. Nutr.*, 45(1): 1–6.

Bainbridge, W.S. 2002. Public attitudes toward nanotechnology. *J. Nanoparticle Res.*, 4(6): 561–570.

Balbus, J., Maynard, A., Colvin, V., Castranova, V., Daston, G., Denison, R., Dreher, K., Goering, P., Goldberg, A., Kulinowski, K., Monteiro-Riviere, N., Oberdorster, G., Omenn, G., Pinkerton, K., Ramos, K., Rest, K., Sass, J., Silbergeld, E. & Wong, B. 2007. Meeting report: Hazard assessment for nanoparticles – Report from an interdisciplinary workshop. *Environ. Health Perspect.,* 115(11): 1654–1659.

Ballou, B., Lagerholm, B.C., Ernst, L.A., Bruchez, M.P. & Waggoner, A.S. 2004. Noninvasive imaging of quantum dots in mice. *Bioconjug. Chem.,* 15(1): 79–86.

BfR. 2006. *Bundesinstitut für Risikobewertung*, Consumer Conference on Nanotechnology in Foods, Cosmetics and Textiles, 20 November 2006.
http://www.bfr.bund.de/cm/245/bfr_consumer_conference_on_nanotechnology_in_foods_cosmetics_and_textiles.pdf

Bin Hussein, M. Z., Yahaya, A. H., Zainal, Z. & Kian, L. H. 2005. Nanocomposite-based controlled release formulation of an herbicide, 2,4-dichlorophenoxyacetate incapsulated in zinc-aluminium-layered double hydroxide. *Sci. Tech. Adv. Mat.,* 6(8): 956–962.

Bouwmeester, H., Dekkers, S., Noordam, M., Hagens, W., Bulder, A., de Heer, C., ten Voorde, S., Wijnhoven, S. & Sips, A. 2007. *Health impact of nanotechnologies in food production. Report 2007.014.* Wageningen, UR, RIKILT – Institute of Food Safety, and National Institute of Public Health & the Environment; Center for Substances and Integrated Risk Assessment.

Bouwmeester, H., Dekkers, S., Noordam, M.Y., Hagens, W.I., Bulder, A.S., de Heer, C., ten Voorde, S.E.C.G., Wijnhoven, S.W.P., Marvin, H.J.P. & Sips, A.J.A.M. 2009. Review of health safety aspects of nanotechnologies in food production. *Reg. Toxicol. Pharmacol.*, 53: 52–62.

Boxall, A.B.A., Chaudhry, Q., Sinclair, C., Jones, A., Aitken, R., Jefferson, B., and Watts, C. 2007. *Current and predicted environmental exposure to engineered nanoparticles.* Central Science Laboratory, York. http://randd.defra.gov.uk/Document.aspx?Document=CB01098_6270_FRP.pdf

Bozeman, B. & Sarewitz, D. 2005. Public values and public failure in U.S. science policy. *Sci. Pub. Policy* 32(2): 119–136.

Breakwell, G.M. & Barnett, J. 2001. The impact of social amplification of risk on risk communication. U.K. HSE. Available at: http://www.hse.gov.uk/research/crr_pdf/2001/crr01332.pdf

Burri, R.V. & Bellucci, S. 2008. Public perception of nanotechnology. *J. Nanoparticle Res.,* 10(3): 387–391.

Buzea, C., Pacheeco, I.I. & Robbie, K. 2007. Nanomaterials and nanoparticles: Sources and toxicity. *Biointerphases,* 2(4): DOI: 10.1116/1.2815690. Available at:
http://scitation.aip.org/getpdf/servlet/GetPDFServlet?filetype=pdf&id=BJIOBN00000200000400MR17000001&idtype=cvips Accessed on September 14, 2009.

Carretaro, M.I. 2002. Clay minerals and their beneficial effects upon human health: A review. *Appl. Clay Sci.*, 21: 155–163.

Cedervall, T., Lynch, I., Lindman, S., Berggard, T., Thulin, E., Nilsson, H., Dawson, K. & Linse, S. 2007a. Understanding the nanoparticle-protein corona using methods to quantify exchange rates and affinities of proteins for nanoparticles. *Proc. Natl. Acad. Sci. USA,* 104(7): 2050–2055.
Cedervall, T., Lynch, I., Foy, M., Berggard, T., Donnelly, S.C., Cagney, G., Linse, S. & Dawson, K.A. 2007b. Detailed identification of plasma proteins adsorbed on copolymer nanoparticles. *Angew Chem. Int. Ed. Engl.*, 46(30): 5754–5756.
Chaudhry, Q., Boxall, A., Aitken, R. & Hull, M. 2005. *A scoping study into the manufacture and use of nanomaterials in the UK.* York, Central Science Laboratory. http://www.defra.gov.uk/science/Project_Data/DocumentLibrary/CB01070/CB01070_3156_FRP.doc Accessed on February 25, 2009.
Chaudhry, Q., Scotter, M., Castle, L., Blackburn, J., Boxall, A., Aitken, R. & Ross, B. 2007. Assessment of the potential use of nanomaterials as food additives or food ingredients in relation to consumer safety and implication for regulatory controls. Final Report on Project A01057, London, Food Standards Agency. 36 pp.
Chaudhry, Q., Scotter, M., Blackburn, J., Ross, B., Boxall, A., Castle, L., Aitken, R. & Watkins, R. (2008) Applications and implications of nanotechnologies for the food sector. *Food Add. Contam*., 25(3): 241–258.
Chen, M., Singer, L., Scharf, A. & von Mikecz, A. 2008. Nuclear polyglutamine-containing protein aggregates as active proteolytic centers. *J. Cell Biol.*, 180(4): 697–704.
Choy, J.-H., Choi, S.-J., Oh, J.-M. & Park, T. 2007. Clay minerals and double layered hydroxides for novel biological applications. *Appl. Clay Sci*., 36: 122–132.
Cientifica. 2006. *Nanotechnologies in the food industry*, published August 2006. Available at: www.cientifica.com/www/details.php?id=47.
Codex. 2007a. *Procedural manual*, 17th Edition. Codex Alimentarius Commission. Rome. ftp://ftp.fao.org/Codex/Publications/ProcManuals/Manual_17e.pdf
Codex. 2007b. *Working principles for risk analysis for food safety for application by governments.* CAC/GL 62-2007. Codex Alimentarius Commission. Rome.
Commission on Risk Assessment and Risk Management in the Federal Government. 1997. *Framework for environmental health risk management*. http://www.riskworld.com/nreports/1997/risk-rpt/pdf/EPAJAN.PDF
Consumers Talk Nano Dialogue. 2007. *Project on emerging nanotechnologies and Consumers Union*. Accessed April 2008. http://www.webdialogues.net/cs/pen-consumer-home/view/di/95?x-t=home.view
COT. 2005. *Joint statement on nanomaterial toxicology.* UK Committees on Toxicity, Mutagencity, and Carcinogenicity of chemicals in food, consumer products and the environment (COT, COM, COC). http://www.food.gov.uk/multimedia/pdfs/cotstatements2005nanomats.pdf
COT. 2007. *COT Addendum to joint statement of the Committees on toxicity, mutagenicity and carcinogenicity of nanomaterial toxicology. COT Statement 2007/01, March 2007.* UK Committees on Toxicity, Mutagencity, and Carcinogenicity of chemicals in food, consumer products and the environment (COT, COM, COC). http://cot.food.gov.uk/pdfs/cotstatementnanomats200701.pdf
Council of Canadian Academies. 2008. *Small is different: A science perspective on the regulatory challenges of the nanoscale.* Report of the Expert Panel on Nanotechnology. Ottawa, ON.
Currall, S.C., **King, E.B**., **Lane, N**., **Madera, J**. **& Turner, S**. 2006. What drives public acceptance of nanotechnology? *Nature Nanotechnol*., 1: 153–155.
Cyras, V.P., Manfredi, L.B., Ton-That, M.-T. & Vázquez, A. 2008. Physical and mechanical properties of thermoplastic starch/montmorillonite nanocomposite films. *Carbohydr. Polym*., 73:55–63.
Davis, J.M. 2007. How to assess the risks of nanotechnology: learning from past experience. *J. Nanosci. Nanotech*., 7: 402–409.
Defra (Department for Environment, Food and Rural Affairs). 2007. Characterising the potential risks posed by engineered nanoparticles – a second UK Government research report. London, HM Government. www.defra.gov.uk
De Jong, W.H., Hagens, W.I., Krystek, P., Burger, M.C., Sips, A.J. & Geertsma, R.E. 2008. Particle size-dependent organ distribution of gold nanoparticles after intravenous administration. *Biomaterials*, 29(12): 1912–1919.

des Rieux, A., Fievez, V., Garinot, M., Schneider, Y.J. & Preat, V. 2006. Nanoparticles as potential oral delivery systems of proteins and vaccines: a mechanistic approach. *J. Control. Release*, 116(1): 1–27.
Donaldson, K. & Borm, P. 2004. Particle and Fibre Toxicology, a new journal to meet a real need. *Part. Fibre Toxicol.,* 1(1): 1.
Donaldson, K., Stone, V., Clouter, A., Renwick, L. & MacNee, W. 2001. Ultrafine particles. *Occup. Environ. Med*., 58(3): 211–216. 199.
Donaldson, K., Aitken, R., Tran, L., Stone, V., Duffin, R. & Forrest, G., *et al.* 2006. Carbon nanotubes: a review of their properties in relation to pulmonary toxicology and workplace safety. **Toxicol. Sci**., 92: 5–22.
Douglas, M. 1992. *Risk and blame: essays in cultural theory*. London, New York, Routledge.
Douglas, M. 1996. *Thought and style: critical essays on good taste*. London, Sage Publications. 240 pp.
Douglas, M. & Wildavsky, A.B. 1982. *Risk and culture: An essay on the selection of technical and environmental dangers*. Berkeley, University of California Press.
Duffin, R., Clouter, A., Brown, D., Tran, C.L., MacNee, W., Stone, V. & Donaldson, K. 2002. The importance of surface area and specific reactivity in the acute pulmonary inflammatory response to particles. *Ann. Occup. Hyg.,* 46(Suppl 1): 242–245.
DuPont. 2007. *NanoRisk framework case study. DuPont light stabilizer*. Available at http://nanoriskframework.org/page.cfm?tagID=1326. Accessed May 6, 2009.
ECOTOC (European Centre for Ecotoxicology and Toxicology of Chemicals). 2006. *Synthetic amorphous silica*. JACC Report, No. 51, CAS No. 7631-86-9.
EFSA (European Food Safety Authority). 2008. *Opinion: Safety of synthetic lycopene: Scientific Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies (Question No EFSA-Q-2007-119)*, Adopted on 10 April 2008.
EFSA (European Food Safety Authority). 2009. *Scientific Opinion on 'The Potential Risks Arising from Nanoscience and Nanotechnologies on Food and Feed Safety', Scientific Opinion of the Scientific Committee*, adopted on 10 February 2009, *EFSA J*., 958: 1–39.
Environmental Defense Fund & Dupont Nano Partnership. 2007. Nanorisk framework. Available at http://www.nanoriskframework.com, Accessed March 4, 2009.
ETC Group. 2004. *Food Packaging Using Nanotechnology Methods: an Overview of 'Smart Packaging' and 'Active Packaging'*. http://www.azonano.com/Details.asp?ArticleID=1317
FAO. 2006. *Food safety risk analysis: a guide for national food safety authorities*. Food and Nutrition Paper 87. Rome, WHO and FAO. Available at: ftp://ftp.fao.org/docrep/fao/009/a0822e/a0822e00.pdf
FAO/WHO. 1995a. *Application of risk analysis to food standards issues*. Report of the Joint **FAO/WHO.** 1995b. Expert Consultation, Geneva, Switzerland, 13–17 March 1995. pp. 1–43, WHO/FNU/FOS/95.3. http://www.who.int/foodsafety/publications/micro/en/march1995.pdf
FAO/WHO. 1997. *Risk management and food safety*. Report of a Joint FAO/WHO Consultation, Rome, Italy, 27–31 January 1997, FAO Food and Nutrition Paper 65. 1-32. Rome, FAO. ftp://ftp.fao.org/docrep/fao/w4982e/w4982e00.pdf
FAO/WHO. 2006. *Food and nutrition paper 87: Food safety risk analysis*.
http://www.fao.org/docrep/012/a0822e/a0822e00.htm
FDA. 2007. *Nanotechnology task force report*.
http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/NanotechnologyTaskForceReport2007/default.htm
Feynman, R. 1959 *There's plenty of room at the bottom*. Available at:
www.its.caltech.edu/~feynman/plenty.html
Finucane, M. L., Alhakami, A., Slovic, P. & Johnson, S. M. 2000. The affect heuristic in judgments of risks and benefits. *J. Behav. Dec. Making*, 13: 1–17.
Fischhoff, B., Slovic, P., Lichtenstein, S., Read, S. & Combs, B. 1978. How safe is safe enough? A psychometric study of attitudes towards technological risks and benefits. *Policy Sci*., 9(2): 127–152.
Florence, A.T. 1997. The oral absorption of micro- and nanoparticulates: neither exceptional nor unusual. *Pharm. Res*., 14: 259–266.
Florence, A.T. 2005. Nanoparticle uptake by the oral route: Fulfilling its potential? *Drug Disc. Today Tech.*, 2(1): 75–81.

FoE (Friends of the Earth). 2008. *Out of the laboratory and on to our plates. Nanotechnology in Food and Agriculture.* A report prepared for Friends of the Earth Australia, Friends of the Earth Europe and Friends of the Earth United States and supported by Friends of the Earth Germany. pp. 1-73, March 2008, http://nano.foe.org.au.
Food Safety Authority of Ireland. 2008. *The relevance for food safety of applications of nanotechnology in the food and feed industries.* Dublin, Food Safety Authority of Ireland. 88 pp.
Frederiksen, H. K., Kristensen, H. G. & Pedersen, M. 2003. Solid lipid microparticle formulations of the pyrethroid gamma-cyhalothrin-incompatibility of the lipid and the pyrethroid and biological properties of the formulations. *J. Control. Release*, 86(2-3): 243–52.
Fujita, Y. 2006. Perception of nanotechnology among general public in Japan. *Asia Pacific Nanotech Weekly*, 4(6).
Garland, A. (ed). 2004. *Nanotechnology in plastics packaging. Commercial applications in nanotechnology*. UK, Pira International Limited UK. pp. 14 -63.
Gardea-Torresdey, J.L., Parsons, J.G., Dokken, K., Peralta-Videa, J., Troiani, H.E., Santiago, P. & Jose-Yacaman, M. 2002. Formation and growth of Au nanoparticles inside live alfalfa plants. *Nano Lett.,* 2: 397–401.
Gardea-Torresdey, J.L., Gomez, E., Peralta-Videa, J., Parsons, J.G., Troiani, H.E. & Jose-Yacaman, M. Alfalfa sprouts: a natural source for the synthesis of silver nanoparticles. *Langmuir*, 19: 1357–1361.
Gaskell, G., Ten Eyck, T., Jackson, J. &Veltri, G. 2005. Imagining nanotechnology: cultural support for technological innovation in Europe and the United States. *Public Underst. Sci*., 14(1): 81–90.
Gatti, A S. & Montanari, S. 2008. *Nanopathologies: The health impact of nanoparticles*. Singapore, PanStanford Publishing . pp. 1–298.
Gatti, A.M., Ballestri, M. & Cappelli, G. 2008a. *Nanoparticles: potential toxins for the organism and the kidney ? Critical care nephrology*, *Basic physiology*, 2nd edition. Philadelphia, USA: Elsevier, pp. 205–218. **Gatti, A., Kirkpatrick, J., Gambarelli, A., Capitani, F., Hansen, T., Eloy, R. & Clermont, G.** 2008b. ESEM evaluations of muscle/nanoparticles interface in a rat model. *J. Material Sci. Med.*, 19(4): 1515–1522.
Gatti, A.M., Tossini, D., Gambarelli, A., Montanari, S. & Capitani, F. 2009. Investigation of the presence of inorganic micro- and nanosized contaminants in bread and biscuits by environmental scanning electron microscopy. *Crit. Rev. Food Sci. Nutr.,* 49(3): 275–282.
Gavelin, K., Wilson, R. & Doubleday, R. 2007. *Democratic technologies?* The final report of the Nanotechnology Engagement Group (NEG), Involve 2007. http://83.223.102.125/involvenew/mt/
Gigerenzer, G. 2003. *Reckoning with risk: learning to live with uncertainty*. Penguin. London. 320 pp.
Graveland-Bikker, J.F. & de Kruif, C.G. 2006. Unique milk protein-based nanotubes: Food and nanotechnology meet.*Trends Food Sci. Technol.* 17: 196–203.
Groves, K. 2008. Potential benefits of micro and nano technology for the food industry: does size matter? *New Food Mag*., 4: 49–52.
Guston, D. & Sarewitz, D. 2002. Real-time technology assessment. *Technol. Soc*., 23: 93–109.
Gyawali, D. 2001. *Water in Nepal*. Katmandou, Hymal Books.280 pp.
Hagens, W.I., Oomen, A.G., de Jong, W.H., Cassee, F.R. & Sips, A.J. 2007. What do we (need to) know about the kinetic properties of nanoparticles in the body? *Regul. Toxicol. Pharmacol*., 49(3): 217–229.
Han, M., Gao, X., Su, J.Z. & Nie, S. 2001. Quantum-dot-tagged microbeads for multiplexed optical coding of biomolecules. *Nat. Biotechnol*., 19: 631–635.
Handy, R.D., Henry, T.B., Scown, T.M., Johnston, B.D. & Tyler, C.T. 2008. Manufactured nanoparticles: their uptake and effects on fish – a mechanistic analysis. *Ecotoxicology*, 17: 396–409.
Hansen T., Clermont G., Alves, A., Eloy, R., Brochhausen, C., Boutrand, J.P., Gatti, A. & Hanssen, L. & van Est, R. 2004. *The double message of nanotechnology: research into rising public perceptions.* Den Haag, Rathenau Institute, October 2004.
Kirkpatrick, J. 2006. Biological tolerance of different materials in bulk and nanoparticulate form in a rat model: Sarcoma development by nanoparticles. *J. R. Soc. Interface*, 3: 767–775.

Harris, A.T. & Bali, R. 2008. On the formation and extent of uptake of silver nanoparticles by live plants. *J. Nanopart. Res.*, 10: 691–695.
Hart Research Associates. 2006. *Report findings, conducted on behalf of the Woodrow Wilson International Center for Scholars, project on emerging nanotechnologies*. New York, Woodrow Wilson International Center for Scholars.
Hart Research Associates. 2007. *Awareness of and attitudes toward nanotechnology and federal regulatory agencies: a report of findings based on a national survey of adults*. Conducted on behalf of the Project on Emerging Nanotechnologies. New York, Woodrow Wilson International Center for Scholars.
Helmut Kaiser Consultancy. 2004. *Study: nanotechnology in food and food processing industry worldwide 2003–2006–2010–2015.* Available at: www.hkc22.com/Nanofood.html
Hillery, A.M., Jani, P.U. & Florence, A.T. 1994. Comparative, quantitative study of lymphoid and non-lymphoid uptake of 60 nm polystyrene particles. *J. Drug Target.*, 2(2): 151–156.
Hillyer, J.F. & Albrecht, R.M. 2001. Gastrointestinal persorption and tissue distribution of differently sized colloidal gold nanoparticles. *J. Pharmaceut. Sci.*, 90(12): 1927–1936.
Hoet, P.H.M., Brüske-Hohlfeld, I. & Salata, O.V. 2004. Nanoparticles: known and unknown health risks. *J. Nanobiotechnol.*, 2: 12.
Hoffman, A. 2009. Shades of green. *Stanford Soci. Innov. Rev.*, Spring: 40–49.
Holbrook, D., Murphy, K., Morrow, J. & Cole, K. 2008. Trophic transfer of nanoparticles in a simplified invertebrate food web. *Nature Nanotechnol.,* 3: 352–355.
ICON (International Council on Nanotechnology). 2008. *Toward predicting nano-biointeractions: an international assessment of nanotechnology environment, health and safety research needs*. Rice University, Houston, Texas: International Council on Nanotechnology, Number 4, May 1, 2008. http://cohesion.rice.edu/CentersAndInst/ICON/emplibrary/ICON_RNA_Report_Full.pdf
IFST (Institute of Food Science and Technology Trust Fund). 2006. *Nanotechnology information statement.* www.ifst.org/uploadedfiles/cms/store/attachments/nanotechnology.pdf. Accessed on 5 July 2009.
IRGC. 2005. *Risk Governance toward an integrative framework.* White Paper No. 1. Geneva.
IRGC. 2006. *Nanotechnology and risk governance*. White Paper No. 2. Geneva.
IRGC. 2008. *Risk governance of nanotechnology applications in food and cosmetics.* Geneva.
ISO. 2008. *Nanotechnologies – Terminology and definitions for nano-objects: Nanoparticle, nanofibre and nanoplate.* Reference number ISO/TS 27687:2008(E). Geneva: International Organization for Standardization.
Jani, P.U., McCarthy, D.E. & Florence, A.T. 1994. Titanium dioxide (rutile) particle uptake from the rat GI tract and translocation to systemic organs after oral administration. *Int. J. Pharmaceut.*, 105(2): 157–168.
Jani, P., Halbert, G.W., Langridge, J. & Florence, A.T. 1990. Nanoparticle uptake by the rat gastrointestinal mucosa: quantitation and particle size dependency. *J. Pharm. Pharmacol*., 42(12): 821–826.
JECFA. 1995. *Evaluation of certain food additives and contaminants*. 44th Report of the FAO/WHO Joint Expert Committee on Food Additives, Geneva.
John, T.A., Vogel, S.M., Minshall, R.D., Ridge, K., Tiruppathi, C. & Malik, A.B. 2001. Evidence for the role of alveolar epithelial gp60 in active transalveolar albumin transport in the rat lung. *J. Physiol.* 533(Pt 2): 547–559.
John, T.A., Vogel, S.M., Tiruppathi, C., Malik, A.B. & Minshall, R.D. 2003. Quantitative analysis of albumin uptake and transport in the rat microvessel endothelial monolayer. *Am. J. Physiol. Lung Cell Mol. Physiol.* 284 .(1): L187–L196.
Ju-Nam, Y. & Lead, J.R. 2008. Manufactured nanoparticles: An overview of their chemistry interactions and potential environmental implications. *Sci. Total Environ*., 400: 396–414.
Kahan, D.M., Slovic, P., Braman, D., Gastil, J. & Cohen, G.L. 2007a. *Affect, values, and nanotechnology risk perceptions: an experimental investigation*. Cultural Cognition Project Working Paper No. 22 (Last accessed through the Social Science Research Network at: http://ssrn.com/abstract=968652 on 19 May 2009).

Kahan, D., Slovic, P., Braman, D., Gastil, J. & Cohen, G. 2007b. *Nanotechnology risk perceptions: the influence of affect and values*. Cultural Cognition Project at Yale and Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars, March 2007.
Kahan, D., Slovic, P., Braman, D., Gastil, J., Cohen, G. & Kyser, D. 2008. *Biased assimilation, polarization, and cultural credibility: an experimental study of nanotechnology risk perceptions*. Project on Emerging Nanotechnologies Brief 3, Woodrow Wilson International Center for Scholars, February 2008.
Kasperson, R.E., Renn, O., Slovic, P., Brown, H.S., Emel, J.,Goble, R., Kasperson, J.X. & Ratick, S. 1988. The social amplification of risk: a conceptual framework. *Risk Analysis,* 8: 177–187.
Kim, Y.S., Kim, J.S., Cho, H.S., Rha, D.S., Kim, J.M., Park, J.D., Choi, B.S., Lim, R., Chang, H.K., Chung, Y.H., Kwon, I.H., Jeong, J., Han, B.S. & Yu, I.J. 2008. Twenty-eight-day oral toxicity, genotoxicity, and gender-related tissue distribution of silver nanoparticles in Sprague-Dawley rats. *Inhal. Toxicol.* 20(6): 575–583.
Kishimoto, A. 2007. *Public acceptance and commercialization of nanotechnology products in Japan.* Presented at the Society for Risk Analysis Annual Meeting 2007 for the National Institute of Advanced Industrial Science and Technology (AIST).
Kishimoto, A. 2008. *Current status of public acceptance and risk governance of nanomaterials in Japan*. Presented at the 2nd World Congress on Risk Society for Risk Analysis, Guadalajara, Mexico.
Kleinman, D. and Powell, M. (eds) 2005. *Madison Area Citizen Consensus Conference on Nanotechnology*. Madison, WI, 24 April 2005, University of Wisconsin.
www.nanocafes.org/files/consensus_conference_report.pdf
Kumar, S.R., Ahmed, V.P.I., Parameswaran, V., Sudhakaran, R., Babu, V.S. & Hameed, A.S. 2008. Potential use of chitosan nanoparticles for oral delivery of DNA vaccine in Asian sea bass (*Lates calcarifer*) to protect from *Vibrio* (*Listonella*) *anguillarum*. *Fish & Shellfish Immunol*., 25: 47–56.
Kuzma, J. & VerHage, P. 2006. *Nanotechnology in agriculture and food production: anticipated applications.* Project on Emerging Nanotechnologies. Washington DC, Woodrow Wilson International Center for Scholars, September 2006
Kuzma, J., Romanchek, J. & Kokotovich, A. 2008. Upstream oversight assessment for agrifood nanotechnology. *Risk Anal*., 28: 1081–1098.
Landry, F.B., Bazile, D.V., Spenlehauer, G., Veillard, M. & Kreutera, J. 1998. Peroral administration of ^{14}C-poly(D,L-lactic acid) nanoparticles coated with human serum albumin or polyvinyl alcohol to guinea pigs. *J. Drug Target.* 6(4): 293–307.
Lee, J. 2006. *Global nanotechnology advocacy by NGOs*. Programme on NGOs and Civil Society, Center for Applied Studies in International Negotiations.
Lewinski, N., Colvin, V. & Drezek, R. 2008. Cytotoxicity of nanoparticles. *Small*, 4(1): 26–49.
Lin, D. & Xing, B. 2009. Root uptake and phytotoxicity of ZnO nanoparticles. *Environ. Sci. Technol*., 42(15): 5580–5585.
Liu, F., Wen, L.X., Li, Z.Z., Yu, W., Sun, H.Y. & Chen, J.F. 2006. Porous hollow silica nanoparticles as controlled delivery system for water-soluble pesticide. *Mat. Res. Bull*., 41(12): 2268–2275.
Luykx, D.M.A.M., Peters, R.J.B., van Ruth, S.M., Bouwmeester, H. 2008. A review of analytical methods for the identification and characterization of nano delivery systems in food. *J. Agric. Food Chem.*, 56(18): 8231–8247.
Lynch, I. & Dawson, K. A. 2008. Protein-nanoparticle interactions. *Nano Today,* 3(1-2): 40–47.
Lynch, I., Dawson, K. A. & Linse, S. 2006. Detecting cryptic epitopes created by nanoparticles. *Sci STKE*, 327: 14.
MacKenzie, A.A. 2007. Looking to the future: potential nanotechnology applications in animal health. *OIE Bull*., 4: 11–14.
Maclurcan, D.A. 2009. Southern roles in global nanotechnology innovation: perspectives from Thailand and Australia. *Nanoethics*, Published online.
http://www.springerlink.com/content/0262rx742qu49507/fulltext.pdf
Macoubrie, J. 2005. *Informed public perceptions of nanotechnology and trust in government*. Project on Emerging Nanotechnologies, New York, Woodrow Wilson International Center for Scholars.

Maynard, A.D. 2002. Estimating aerosol surface area from number and mass concentration measurements. *Ann. Occup. Hyg*., 47(2): 123–144.
Maynard, A.D. 2006. *Nanotechnology: A research strategy for addressing risk*. Washington, DC: Project on Emerging Nanotechnologies.
Maynard, A.D. & Kuempel, E.D. 2005. Airborne nanostructured particles and occupational health. *J. Nanopart. Res*., **7**(6): 587–614.
Morris, V. J. 2008. Nanotechnology in the food industry. *New Food Mag*., 4: 53–55
Mukal, D., Sexena, N. & Dwivedi, P.D. 2009. Emerging trends of nanoparticles application in food technology: safety paradigms. *Nanotoxicology*, 3(10): 10–18.
Murr, L.E. 2009. Nanoparticulate materials in antiquity: The good, the bad and the ugly. *Mat. Charac.,* 60: 261–270.
Nano Jury UK. 2005. *Our provisional recommendations, September 2005*. http://www.greenpeace.org.uk/files/pdfs/migrated/MultimediaFiles/Live/FullReport/7249.pdf
National Science and Technology Council, Committee on Technology, Subcommittee on Nanoscale Sceince, Engineering and Technology, Nanotechnology, Environmental and Health Implications (NEHI) Working Group. 2008. *National nanotechnology initiative, strategy for environmental health and safety research*. Washington, DC: National Science and Technology Council. Available at: http://www.nano.gov/NNI_EHS_Research_Strategy.pdf
Nel, A., Xia, T., Madler, L. & Li, N. 2006. Toxic potential of materials at the nanolevel. *Science*, 311(5761): 622–627.
NISENet. 2009. NISE Network Forum: risks, benefits, and who decides? E. Kunz, C. Reich, and A. Lindgren-Streicher, eds. Available online at http://www.nisenet.org/catalog/assets/documents/nise-network-forum-quotrisks-benefits-who-decidesquot
Nowack, B. & Bucheli, T. 2007. Occurrence, behavior and effects of nanoparticles in the environment. *Environ. Poll*., 150: 5–22.
NRC. 1996. *Understanding risk: informing decisions in a democratic society*. www.nap.edu. Washington, DC, NRC.
NRC. 2006. *A matter of size: a triennial review of the US National Nanotechnology Initiative*. National Research Council, US National Academies, Washington DC, National Academy Press.
NRC. 2008. Review of the Federal Strategy for nanotechnology-related environmental, health, and safety research. Washington DC, National Academy Press.
Oberdörster, G., Maynard, A., Donaldson, K., Castranova, V., Fitzpatrick, J., Ausman, K., Carter, J., Karn, B., Kreyling, W., Lai, D., Olin, S., Monteiro-Riviere, N., Warheit, D. & Yang, H. 2005a. Principles for characterizing the potential health effects from exposure to nanomaterials: elements of a screening strategy. *Particle Fibre Toxicol*., 2: 8.
Oberdörster, G., Oberdörster, E. & Oberdörster, J. 2005b. Nanotoxicology: an emerging discipline evolving studies of ultrafine particles. *Environ. Health Perspect*., 113(7): 823–839.
Oberdorster, G., Stone, V. & Donaldson, K. 2007. Toxicology of nanoparticles: a historical perspective. *Nanotoxicology*, 1(1): 2–25.
Ochoa, J., Irache, J.M., Tamayoa, I., Walz, A., DelVecchio, V.G. & Gamazoa, C. 2007. Protective immunity of biodegradable nanoparticle-based vaccine against an experimental challenge with *Salmonella* Enteritidis in mice. *Vaccine*, 25: 4410–4419.
OECD (Organisation for Economic Co-operation and Development). 2008a. Manufactured nanomaterials: Work programme 2006-2008. *In OECD Environment, Health and Safety Publications. Series on the safety of manufactured nanoparticles*. Number 4. pp. 1–17, February 2008. ENV/JM/MONO(2008)2. Paris, OECD. www.oecd.org
OECD (Organisation for Economic Co-operation and Development). 2008b. List of manufactured nanomaterials and list of endpoints for phase one of the OECD testing programme. *In OECD Environment, Health and Safety Publications*. *Series on the safety on manufactured nanomaterials.* Number 6. pp. 1–13, 7 July 2008. ENV/JM/MONO(2008)13/REV. Paris, OECD. www.oecd.org
O'Neil, M. & Ackland, R. 2006. *The structural role of nanotechnology – opposition to online environmental activist networks*. Presented at the International Sunbelt Social Network Conference, Vancouver, Canada.
Pan, J,-F., & Wang, W.-X. 2004. Differential uptake of dissolved and particulate organic carbon by the mussel *Perna viridis*. *Limnol. Oceanogr*., 49(6): 1980–1991.

Panté, N. & Kann, M. 2002. Nuclear pore complex is able to transport macromolecules with diameters of ~39 nm. *Mol. Biol. Cell.,* 13(2): 425–34.
Park, B.K., Kim, D., Jeong, S., Moon, J. & Kim, J.S. 2007. *Thin solid films*, 7/16. Vol. 515, No. 19, pp. 7706–7711.
Park, K.H. (2006) Patent Application: WPI ACC NO: 2006-489267/200650 *Preparation method antibacterial wheat flour by using silver nanoparticles*. Korea.
Parr, D. 2006. Survey response. In *Survey on nanotechnology governance*, Roco, M.C., Litten, E. (eds) IRGC Working Group on Nanotechnology. pp. 46-48.
Peters K, Unger, R., Gatti, A., Sabbioni, E., Gambarelli, A. & Kirkpatrick, J. 2006. *Impact of ceramic and metallic nanoscaled particles on endothelial cell functions in vitro*. Nanotechnologies for the Life Sciences, Vol. 5 Nanomaterials- Toxicity, Health and Environmental Issues, ed. Challa, S.S., Kumar, Weinheim, DE: R. Wiley–VCH Verlag GmbH &Co. KGaA 2006. ISBN: 3-527-31385-0, vol 5, pp. 108–125.
Peters, K., Unger R.E., Gatti, A.M., Sabbioni, E., Tsaryk, R. & Kirkpatrick, C.J. 2007. Metallic nanoparticles exhibit paradoxical effects on oxidative stress and pro-inflammatory response in endothelial cells in vitro. *Int. J. Immunopathol. Pharmacol*., 20(4): 685–695
Pidgeon, N., Kasperson, R. & Slovic, P. 2003. *The social amplification of risk*. Cambridge, Cambridge University Press.
Powell, J.J., Harvey, R.S.J., Ashwood, P., Wolstencroft, R., Gershwin, M.E. & Thompson, R.P.H. 2000. Immune potentiation of ultrafine dietary particles in normal subjects and patients with inflammatory bowel disease. *J. Autoimmunity*, 14: 99–105.
Powers, K., Brown, S., Krishna, V., Wasdo, S., Moudgil, B. & Roberts, S. 2006. Research strategies for safety evaluation of nanomaterials. Part VI. Characterization of nanoscale particles for toxicological evaluation. *Toxicol. Sci.,* 90(2): 296–303.
Priest, S. 2006. The North American opinion climate for nanotechnology and its products: opportunities and challenges. *J. Nanopart. Res*., 8: 563–568.
Roco, M.C. & Bainbridge, W.S. (eds) 2001. *Societal implications of nanoscience and nanotechnology*. Boston, Kluwer Academic Publishers. pp. 3–4.
Rose, J., Thill, A. & Brant, J. 2007. Methods for structural and chemical characterization of nanomaterials. *In: Environmental nanotechnology. Applications and impacts of nanomaterials*. New York, NY: McGraw Hill, ISBN: 9780071477505, pp. 105–154.
Roszek, B., de Jong, W. & Geertsma, R. 2005. *Nanotechnology in medical applications: State-of-the-art in materials and devices*. RIVM report. 265001001/2005. The Netherlands: National Institute for Public Health and the Environment.
Rowe, G. & Frewer, L. 2000. Public participation methods: a framework for evaluation. *Sci. Technol. Hum Values*, 25: 3.
Royal Society. 2004. *Nanoscience and nanotechnologies: opportunities and uncertainties*. July 2004. Available at: http://www.nanotec.org.uk/finalReport.htm
Sanguansri, P. & Augustin, M.A. 2006. Nanoscale materials development – a food industry perspective. *Trends Food Sci. Tech*., 17: 547–556.
SSC (Scientific Steering Committee). 2000. *First report on the harmonisation of risk assessment procedures*. pp.1–173. European Commission, Health and Consumer Protection Directorate-General. http://ec.europa.eu/food/fs/sc/ssc/out83_en.pdf
SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks). 2005. *Opinion on the appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies.* Adopted by the SCENIHR during the 7th plenary 28-29 September 2005.
SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks). 2006. *The appropriateness of existing methodologies to assess the potential risks with engineered and adventitious products of nanotechnologies*. Adopted during the 10th plenary 26 March 2006 after public consultation.
SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks). 2007a. *Opinion on the appropriateness of the risk assessment methodology in accordance with the technical guidance documents for new and existing substances for assessing the risks of nanomaterials*. Adopted during the 19th plenary 21–22 June 2007 after public consultation.

SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks). 2007b. *Opinion on the scientific aspects of the existing and proposed definitions relating to products of nanoscience and nanotechnologies*, adopted on 29 November 2007.
Schneider, J.C. 2007. Can microparticles contribute to inflammatory bowel disease: innocuous or inflammatory? *Exp. Biol. Med*., 232: 1–2.
Schulz, C., Obermüller-Jevic, U.C., Hasselwander, O., Bernhardt, J., Biesalski, H.K. 2006. Comparison of the relative bioavailability of different coenzyme Q10 formulations with a novel solubilizate (Solu Q10). *Int. J. Food. Sci. Nutr*., 57(7-8): 546–55.
Shatkin, J.A. 2008. *Nanotechnology health and environmental risks*. Boca Raton, FL, CRC Press.
Siegrist, M., Cousin, M-E., Kastenholz, H. & Wiek, A. 2007. Public acceptance of nanotechnology foods and food packaging: The influence of affect and trust. *Appetite,* 49: 459–466.
Simon, P. & Joner, E. 2008a. Conceivable interactions of biopersistent nanoparticles with food matrix and living systems following from their physicochemical properties. *J. Food Nutr. Res.,* 47(2): 51–59.
Šimon, P., Chaudhry, Q. & Bakoš, D. 2008. Migration of engineered nanoparticles from polymer packaging to food – a physiochemical view. *J. Food Nutr. Res*., 47(3): 105–113.
Singh, R., Pantarotto, D., Lacerda, L., Pastorin, G., Klumpp, C., Prato, M., Bianco, A. & Kostarelos, K. 2006. Tissue biodistribution and blood clearance rates of intravenously administered carbon nanotube radiotracers. *Proc. Natl. Acad. Sci. USA,* 103(9): 3357–3362.
Sjoberg, L. 2006. *Myths: The psychometric paradigm and how they can misinform risk communication*. SSE/EFI Working Paper Series in Business Administration No. 2006:10.
Slovic, P., Fischoff, B. & Lichenstein, S. 1985. Characterizing perceived risk. *In* R.W. Kates, C. Hohenemser & J.X. Kasperson, eds. *Perilous progress: hazards of technology*. Boulder, CO, Westview Press.
Slovic, P., Flynn, J. H. & Layman, M. 1991. Perceived risk, trust, and the politics of nuclear waste. Science, 254: 1603–1607.
Smolander, M., Hurme, E., Koivisto, M. & Kivinen, S. 2004. *PCT International Patent Application* WO 2004/102185 A1, 2004.
Sorrentino, A., Gorrasi, G. & Vittoria, V. 2007. Specialty Biotech Thailand. *Trends Food Sci. Technol*., 18: 84–95. www.sbtthai.com/profile.html
Sozer, N. & Kokini, J.L. 2009. Nanotechnology and its applications in the food sector. *Trends Biotechnol*., 27(2): 82–89.
Spriull, J.C. 2006. *Novel pre-harvest approaches to control enteric food-borne bacteria in poultry*. M.S. thesis, North Carolina State University. 102 pp.
Sustech GMBH & Co. 2003. Patent Application EP20030748025, *Sweet containing calcium*, Germany.
Sustech GMBH & Co. 2004. International Patent Application PCT/EP2003/010213 *Coated chewing gum*, Germany.
Szentkuti, L. 1997. Light microscopical observations on luminally administered dyes, dextrans, nanospheres and microspheres in the pre-epithelial mucus gel layer of the rat distal colon. *J.Contr. Rel.,* 46(3): 233–242.
Tang, S., Zou, P., Xiong, H. & Tang, H. 2008. Effect of nano-SiO_2 on the performance of starch/polyvinyl alcohol blend films. *Carbohydr. Polym*., 72: 521–526.
TA Swiss. 2006. *Public reactions to nanotechnology in Switzerland: Report on Publifocus Discussion Forum, Nanotechnology, Health and Environment*. Switzerland, Centre for Technology Assessment. http://www.ta-swiss.ch/a/nano_pfna/2006_TAP8_Nanotechnologien_e.pdf
Taylor, M. R. 2008. *Assuring the safety of nanomaterials in food packaging: The regulatory process and key issues.* Washington DC, Project on Emerging Nanotechnologies.
Thomas, K. & Sayre, P. 2005. Research strategies for safety evaluation of nanomaterials, Part I: evaluating the human health implications of exposure to nanoscale materials. *Toxicol. Sci.,* 87(2): 316–321.
Thompson, M., Ellis, R. & Wildavsky, A. 1990. *Cultural theory*. Boulder, CO, Westview Press. 296 pp.

Tiede, K., Boxall, A.B.A., Tear, S.P., Lewis, J., David, H. & Hassellöv, M. 2008. Detection and characterization of engineered nanoparticles in food and the environment. *Food Additives & Contaminants,* Part A: *Chemistry, analysis, control, exposure & risk assessment*, 25(7): 795–821.
USDA FSIS. 2001. *Risk assessment of the public health impact of* Escherichia coli *0157:H7 in ground beef*. Prepared by the *Escherichia coli* 0157:H7 Risk Assessment Team. Available online at: http://www.fsis.usda.gov/OPPDE/rdad/FRPubs/00-023N/00-023NReport.pdf
Vartiainen, J., Rättö, M. & Paulussen, S. 2005a. Antimicrobial activity of glucose oxidase-immobilized plasma-activated polypropylene films. *Packaging Technol. Sci.,* 18: 243–251.
Vartiainen, J., Rättö, M., Tapper, U., Paulussen, S. & Hurme, E. 2005b. Surface modification of atmospheric plasma activated BOPP by immobilizing chitosan. *Polym. Bull.,* 54: 343–352.
Wajda, R., Zirkel, J. & Schaffer, T. 2007. Increase of bioavailability of Coenzyme Q10 and Vitamin E. *J. Medic. Food*, 10: 731–734.
Wang, J., Zhou, G., Chen, C., Yu, H., Wang, T., Ma, Y., Jia, G., Gao, Y., Li, B., Sun, J., Li, Y., Jiao, F., Zhao, Y. & Chai, Z. 2007a. Acute toxicity and biodistribution of different sized titanium dioxide particles in mice after oral administration. *Toxicol. Lett.,* 168(2): 176–185.
Wang, L., Li, X., Zhang, G., Dong, J. & Eastoe, J. 2007b. Oil-in-water nanoemulsions for pesticide formulations. *J. Colloid Interface Sci*., 314(1): 230–235.
Weiss, J., Takhistov, P., & McClements, D.J. 2006. Functional materials in food nanotechnology. *J. Food Sci.*, 71(9): R107–R116.
WHO. 1995. Evaluation of certain food additives and contaminants (Forty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 859.
WHO. 2007. Evaluation of certain food additives and contaminants (Sixty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 940.
Wilsdon, J. 2006. Survey response. In *Survey on nanotechnology governance.* Roco, M.C., Litten, E. (eds), IRGC Working Group on Nanotechnology. pp. 29-32.
Wilsdon, J. & Willis, R. 2004. *See-through science*. Available at: www.demos.co.uk Last accessed December 15, 2004.
Wilson, M.J. 2003. Clay mineralogical and related characteristics of geophagic materials. *J. Chem Ecol.*, 29(7): 1525–1547.
Woodrow Wilson International Centre for Scholars. 2009. *The Nanotechnology Consumer Inventory*. Available at: www.nanotechproject.org/inventories/consumer/
YingHua, S., ZiRong, X., JianLei, F., CaiHong, H. & MeiSheng, X. 2005. In vitro adsorption of aflatoxin adsorbing nano-additive for aflatoxin B1, B2, G1, G2. *Scientia Agricultura Sinica*, 38(5): 1069–1072.
Zhang, L., Jiang, Y., Ding, Y., Povey, M. & York, D. 2007. Investigation into the antibacterial behaviour of suspensions of ZnO nanoparticles (ZnO nanofluids). *J. Nanoparticle Res*., 9(3): 479–489.
Zhu, H., Han, J., Xiao, J.Q. & Jin, Y. 2008. Uptake, translocation, and accumulation of manufactured iron oxide nanoparticles by pumpkin plants. *J. Environ. Monit.*, 10: 713–717.
Zhu, X., Zhu, L., Chen, Y. & Tian, S. 2009. Acute toxicities of six manufactured nanomaterial suspensions to *Daphnia*. *J. Nanopart. Res*., 11: 67–75.

Appendices

Appendix 1: Core Group meeting outcome note

Nanotechnology Core Group Meeting: Key Outcomes

14-15 May 2008, FAO HQ, Rome, Italy

Attendees: **Dr Ezzeddine Boutrif** **FAO, Chair**

Collaborators:

Richard Canady	Food and Drug Administration, USA
David Carlander	European Food Safety Authority
Steve Froggett	US Department of Agriculture, USA
Philippe Martin	European Commission
Luiz Mattoso	Empresa Brasileira de Pesquisa Agropecuária, Brazil
Vic Morris	Institute of Food Research, UK
Brian Priestly	Centre for Human Health Risk Assessment, Australia
Alan Reilly	Food Safety Authority of Ireland, Ireland

Secretariat and FAO Staff

Lourdes Costarrica	FAO
Gerald Moy	WHO
Renata Clarke	FAO
Deon Mahoney	FAO
Daniela Battaglia	FAO
Barbara Burlingame	FAO
Annika Wennberg	FAO
YongZhen Yang	FAO
Kazuaki Miyagishima	Codex

Introduction

Mr Boutrif welcomed participants on behalf of FAO and invited all participants to introduce themselves. The Agenda was tabled and adopted by the meeting (Annex 1).
Dr Costarrica provided participants with a copy of the **FAO/WHO Framework on the Provision of Scientific Advice** and an overview which highlighted the principles, practices and procedures that underpin the provision of such advice.
Dr Moy welcomed participants on behalf of WHO and Mr Boutrif provided an overview of the purpose of the Core Group Meeting and the forthcoming **Joint FAO/WHO Expert Meeting on the Application of Nanotechnologies in the Food and Agriculture Sectors: Potential Food Safety Implications.** The WHO representative reminded participants that WHO prefers to have two separate meetings addressing risk assessment and risk management.

Preliminary Comments

Participants exchanged their views regarding the direction and future of nanotechnology and the importance of specific issues that needs to be addressed during the Expert Meeting. These included:

- Nanotechnology applications
- Food contact materials
- Risk assessment methodology
- Risk communication
- Differentiating between naturally occurring nanoparticles and engineered nanoparticles
- The impacts of nanotechnology on the environment and entry of nanomaterials into the food chain e.g. through spent energy crops

- Traceability and monitoring.

It was noted that it is important that the Expert Meeting maintains neutral and scientific attitude towards this enabling technology and the benefits it may bring, rather than focus on hazards and the suspicion of harm that are not science-based.

Themes of the Expert Meeting

Participants initially suggested the four key subject themes for the Expert Meeting:

1) applications of nanotechnology
2) challenges of risk assessment
3) challenges of managing public health and safety risks, and
4) transparency and risk communication challenges.

It was emphasised that nanotechnologies are enabling technologies and there were significant benefits, while there was a view that we could gain wisdom from errors of the past regarding the introduction of new technologies.

Understanding exposure pathways and endpoints was important, and conventional exposure assessment may not work for nanoparticles. Furthermore, there were comments regarding agricultural and veterinary nanotechnology applications, especially the route of transmission in animals, and possible presence in food products.

Nanomaterials may be recycled and could re-enter into the food chain. Life-cycle assessments may be needed for such cases.

Later participants agreed that the Expert Meeting will focus <u>three themes</u>:

1) Existing and expected nanotechnology applications in the food and agriculture sectors
2) Assessment of human health risks associated with the use of nanotechnologies and nanomaterials in the food and agriculture sectors
3) Development of transparent and constructive dialogues among stakeholders

Scope and Objectives

Scope

Initially there was some concern about the perceived size of the task confronting the Expert Meeting, but participants eventually agreed that meeting would take a strategic approach to the topic, and this entails a 'helicopter' view of nanotechnology. The meeting would not delve into the regulatory instruments for management of nanotechnology.

The Core Group agreed:

The scope of the Expert Meeting covers actual and anticipated nanotechnologies with application in the food and agriculture sectors and their potential impact on food safety along the entire food chain.

The meeting will identify:

- any needs for further guidance and scientific advice;
- what needs to be done to better understand any potential food safety risks associated with nanotechnologies applied to the food and agriculture sectors (the form of a 'road map'); and
- further work that may be required to better assess, manage and communicate these risks.

The following areas will provide the main focus for discussion:

- The application of nanotechnologies in food production;
- The application of nanotechnologies in food processing and packaging;
- The use of diagnostic tools, enabled by nanotechnologies and nanoscience, in the food and agriculture sectors; and
- Food safety regulatory framework for the use of nanotechnologies in the food and agriculture sectors.

Issues that are NOT to be covered

The Expert Meeting **will not** address occupational health and safety matters surrounding the use and application of nanotechnologies in the food and agriculture sectors. Environmental issues will not be considered, unless there is a potential impact on food safety through the food chain.

Objectives

- Take stock of actual and anticipated applications of nanotechnologies in the food and agriculture sectors and identify potential food safety implications associated with them.
- Consider the application of current risk assessment methodologies to evaluate the safety of nanomaterials used in the food chain, to determine the need for additional tools or metrics and to identify any data requirements and research gaps.
- Identify and share lessons learned in the management of the safety of foods produced and/or processed using nanotechnologies.
- Advise on ways and means of fostering transparent and trustful dialogue among all stakeholders
- Advise FAO and WHO on their possible roles in promoting sound governance of food safety issues linked to applications of nanotechnologies.

Background Papers

Participants provided advice on the draft outlines for the three background papers for the Expert Meeting and a paper on regulatory issues that FAO will develop. The outlines were to be subsequently revised.

Paper 1:
Participants agreed that the paper 1 includes the definition section to list "working definitions" to be used during the Expert Meeting. The Expert Meeting is not meant to define or propose any "official" terms related to nanotechnologies. If there is a strong need identified during the Expert Meeting to have internationally accepted definitions, the need should be addressed in the report.

Paper 2:
Paper 2 should highlight potential human health impacts of applications of nanotechnology and provide an overview of issues related to the risk assessment of nanoparticles in order to address the potential food safety concerns through specific applications identified in Paper 1.

Paper 3:
Paper 3 should examine available evidence on the concerns and perceptions of stakeholders and make recommendations on the roles of all stakeholder groups to the applications of nanotechnologies in the food and agriculture sectors, in view of stakeholder confidence.

Call for Experts

Participants provided advice on the skills required by experts in the Expert meeting, and for inclusion in the FAO/WHO Call for Experts.

Call for Information

Participants provided advice on the type of information that should be sought in an FAO/WHO Call for Information.

Meeting closed: 5:00pm Thursday 15 May 2008

ANNEX 1 of Appendix 1

Meeting of the Core Group of Experts
14-15 May 2008
FAO Headquarters, Rome, India Room (A327/9)

DAY 1:WEDNESDAY 14th MAY 2008

Time	Activity	Who
9.00am – 10.00am	Welcome and Introductions of Participants	
	Welcoming remarks from FAO – Including FAO/WHO Framework on the Provision of Scientific Advice and the Global Initiative for Food-related Scientific Advice (GIFSA)	Lourdes Costarrica, FAO
	Welcoming remarks from WHO	Gerald Moy, WHO
	Welcome and Opening remarks - Outline of the purpose and goals of the Core Group Meeting	Ezzeddine Boutrif, FAO
	Organizational issues/ housekeeping	Secretariat
10.00am - 11.00am	Preliminary comments and exchange of views by all collaborators. Purpose is to flag key issues in relation to the application of nanotechnology in food and agriculture	Main Facilitator: Ezzeddine Boutrif Lourdes Costarrica
11.00am - 11:30am	**Coffee**	
11.30am - 12.30pm	Discussion on applications of nanotechnology and on the hazards associated with nanoparticles	Main Facilitator: Deon Mahoney
12.30pm – 1.30pm	**Lunch**	
1.30pm – 3:00 pm	Discussion on the challenges of risk assessment and specifically exposure assessment for nanoparticles in food	Main Facilitator: Gerald Moy
3:00 pm – 4:00pm	Discussion on the challenges of managing public health and safety risks associated with nanoparticles in food and agriculture	Main Facilitator: Renata Clarke
4:00pm – 4.30pm	**Coffee**	
4.30pm – 5.30pm	Discussion on transparency and risk communication challenges of nanotechnology applications in the agrifood sector	Main Facilitator: Renata Clarke
5:30pm – 6:00pm	Discussion on Scope and Objectives of Expert Meeting	Main Facilitator: Ezzeddine Boutrif

DAY 2:Thursday 15th May 2008

Time	Activity	Who
8.30am – 9.00am	Recap of Day 1 – Confirmation of Scope and Objectives	Ezzeddine Boutrif
9.00am – 10.30am	Agreeing on Background Papers	
10.30am - 10:45am	**Coffee**	
10.45am - 11.30am	Agreeing on Background Papers **CONTINUED**	
11.30am – 12.30pm	Profile of expertise required at the Expert Meeting	
12.30pm – 1.30pm	**Lunch**	
1.30pm – 2.30pm	Draft Agenda for the Expert Meeting - Review	
2.30pm – 3.00pm	Call for data – Review type of information sought	
3:00pm – 3:30pm	**Coffee**	
3.30pm – 4.30pm	Next steps – ongoing involvement of collaborators	FAO
4:30pm – 5:00pm	Summary and Close	FAO and WHO

Appendix 2: Call for experts and information

Joint FAO/WHO Expert Meeting on the Application of Nanotechnologies in the Food and Agriculture Sectors: Potential Food Safety Implications

(To be held on 1-5 June 2009, at FAO Headquarters, Rome, Italy)

Call for Experts and Call for Information

Background

The Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) have recognized a need for scientific advice on any food safety implications that may arise from the use of nanotechnologies in the food and agriculture sectors through its horizon scanning activities.

FAO and WHO are planning the Joint Expert Meeting to take stock of existing and emerging applications of nanotechnologies in the food and agriculture sectors.

Call for Experts (Deadline for submission: not later than 9 January 2009)

FAO and WHO are now seeking candidates for a roster of experts who should meet requirements mentioned below to have essential knowledge and experience relevant to the use of nanotechnologies in food and agriculture and to the identification and assessment of potential risks.

Qualification required

General requirements

Candidates for the experts should fulfil the following general requirements:

- Advanced university/college degree in analytical chemistry, organic chemistry, biochemistry, physical chemistry, microbiology, food technology, food science, nutrition, toxicology, agronomy, epidemiology, public health, veterinary science, social sciences, or other relevant fields;
- Scientific publications in peer-reviewed journals, in particular, relevant publications within the last ten years;
- Good knowledge of the English language, written and spoken; and
- Leadership or invited participation in national, regional or international scientific bodies, committees, and other expert advisory bodies pertinent to the scope of the Meeting.

Specific requirements

Candidates should meet one or more of the specific requirements outlined below:

- Good technical and scientific knowledge of nanoscience and nanotechnologies (existing and under development) with application in food and agriculture with at least three years' experience working in this field;
- Toxicologist with at least 10 years' experience in food safety risk assessment and with demonstrated involvement in the toxicological evaluation of nanoparticles, including toxicokinetic properties and interactions with biomolecules;
- At least 10 years' experience in exposure assessment within the food safety risk assessment framework with demonstrated involvement in the application of exposure assessment methodologies to nanoparticles in foods, including long-term exposure assessment; and/or.
- Experience, preferably at least five years', in the evaluation/analysis on perceptions among stakeholders (e.g. consumers, producers and manufactures, research communities, regulatory authorities) for using new technologies including nanotechnology that may impact in particular the food and agriculture sectors, for ensuring transparent and constructive dialogue among stakeholders.

In addition, where necessary, experience in food safety management with demonstrated involvement in the management of potential risks associated with the application of new technologies such as nanotechnologies in the food and agriculture sectors, will be considered.

Process for selection of experts

FAO and WHO place great value on the technical quality and independence of the participating experts as well as to the transparency of its selection process. Both organizations have developed well-defined procedures for selecting experts that promote the excellence and independence of opinions provided.

Each applicant's *curriculum vitae* will be reviewed on the basis of the criteria listed above by a selection panel comprising three or more individuals including at least one independent, internationally recognized external expert appointed by FAO and WHO. Based on the evaluation of the selection panel, highly qualified applicants will be included in an expert roster that will be used by FAO and WHO in selecting experts for Meeting.

In selecting experts FAO and WHO will consider, in addition to scientific and technical excellence, diversity and complementarity of professional backgrounds, balanced representation from geographic regions including developing and developed countries as well as gender balance.

Selected experts may be requested to assist in the preparation of background papers.

Appointment of experts

The experts will be invited to participate only in their individual capacity. Experts shall not represent the government of which he or she is a citizen, or the institution with which he or she is associated. The experts designated to participate in such meetings will not receive any remuneration. However, travel costs, subsistence allowance and other related expenses will be the exclusive responsibility of FAO and WHO.

Applications

Interested applicants should submit their *curriculum vitae* including a detailed description of their education, work experience and a list of peer reviewed publications relevant to the topics indicated above. Do not include reprints in your submission unless specifically requested at a later date. Applicants must have a good working knowledge of English as meetings and correspondence will be in English only.

Before participating in meetings, the selected experts will be required to declare any potential interests associated with the subjects and substances that will be evaluated through completion of a standard form developed by FAO and WHO. They will be asked to indicate in writing any interest (financial and intellectual) on their part or their spouse that may affect their scientific independence as experts

including one or more of the following conditions: employment (past or present) by any commercial enterprise or private or civil sector association; a recipient of research or other study grants from such enterprises or associations; or shareholdings in commercial enterprises active in fields related to the subjects and the substances. These declarations will be evaluated and retained by the Joint Secretariats. In addition, a confidentiality undertaking is also to be signed to ensure proper handling of dossiers and proprietary information.

Call for Information (Deadline for submission: not later than 9 January 2009)

FAO/WHO is seeking submissions of published and unpublished technical information to ensure that all relevant information on the use of nanotechnologies in food and agriculture and the potential risks will be considered. The information will form part of the database that will be examined to assure a comprehensive understanding of the technologies, their applications and the potential risks in order to facilitate the development of appropriate and effective recommendations. In particular, FAO/WHO through this call for information would like to raise awareness about the need to make available relevant information that may not be readily available in the public domain.

Confidential and/or unpublished information

FAO and WHO recognize that some of the information and relevant data which is now required may be unpublished or of a confidential nature. With regard to unpublished information and data, this remains the property of the author for subsequent publication by the owner as original material. Unpublished confidential studies that are submitted will be safeguarded in so far as it is possible to do so without compromising the work of FAO and WHO. Specific issues relating to confidentiality should be discussed directly between the information and data owners and FAO/WHO. For these and other issues please contact FAO and WHO at the contacts provided below.

Information requested:

- Current use of nanotechnologies in livestock and crop production, food processing, food packaging and food distribution, including descriptions of the technologies, potential health risks to consumer, benefits to the various stakeholder groups (including the general public);
- On-going research and development on nanotechnologies for use in the food and agriculture sectors that are expected to reach market within the next 10 years including descriptions of the technologies, potential risks, benefits to the various stakeholder groups (including the general public;
- Investigations of nanoparticle migration from food contact materials into foods;
- Purity, particle size distribution and properties of nanoparticulate substances for use in foods and food contact surfaces;
- Available data for a deeper mechanistic understanding of the behaviour of nanoparticles in the body (e.g. toxicokinetics, possible mechanisms of toxicity);
- Information on nano- forms of vitamins and nutrients in relation to their bio-availability, possible interference with the absorption of other nutrients and consideration of safe-limits;
- Available data on interactions of nanoparticles with biomolecules, nutrients and contaminants, and their relevance to human health;
- Available techniques for detecting, characterizing and measuring nanoparticles in foods and food contact materials;
- Risk assessments carried out on nanomaterials for use in foods and food contact surfaces, including case studies and methodologies for assessing human exposure by oral route);
- Information on possible developmental of standardised protocols for the assessment of toxicological profiles of nanoparticles *in vitro* and *in vivo*;
- Information on nano-enabled diagnostic tools in the food (including water) and agriculture sectors;

- Potential needs and priority area for scientific advice in consideration of safety management and regulation at national authorities;
- Reviews, surveys or other information concerning public perceptions of the applications of nanotechnologies to the food and agriculture sectors; and
- Any other relevant information that falls in the scope of the Meeting.

Deadline

Call for experts

Experts' applications should be sent, preferably in electronic means, to the Joint Secretariats by 9 January 2009 to the addresses below. Applications after that date will be evaluated if additional expertise is required and the evaluation and selection will follow the same procedure as described.

Call for information

Information/data should be submitted to the Joint Secretariats by 9 January 2009 to the addresses below, preferably by electronic means, either via e-mail (if not too large) or on CD- ROM).

Appendix 3: Briefing note for participants

About participants

- Experts are invited on the basis of their particular expertise and in their personal capacity.
- Experts' responsibility is to consider the questions posed, review available data, prepare draft evaluations in advance for discussion, draw appropriate conclusions, draft report sections and adopt the final report.
- Resource persons are experts who provide technical support to the joint FAO/WHO secretariat by making the relevant information available for the experts and answering the queries posed by the experts.
- Resource persons provide technical advice during the meeting, but cannot influence the adoption of the final report.
- The Plenary Chairperson and the Plenary Rapporteur are nominated by the joint FAO/WHO secretariat and elected by the participants.
- The Plenary Chairperson is responsible to facilitate and moderate the plenary discussions in a balanced and neutral way, and to ensure the adopted final report reflects consensus of all the experts.
- The Plenary Rapporteur is responsible to take note of all the plenary discussions and to ensure inclusion of key technical elements and references addressed during the discussions.
- Joint FAO/WHO secretariats comprise professional staff members from FAO and WHO, who are responsible for the preparation, organization and appropriate follow-up of the expert meetings.

About resource/information materials

- Hard copies of resource/information materials including responses to "call for information" are available during the meeting at the document desks (Mexico room, Nigeria room and Room B245).
- If you would like to provide additional resource/information materials, contact joint FAO/WHO secretariat before displaying at the document desks.

For the meeting background, workflow, working group assignment, expected outputs of the meeting, please see attached, the introductory slides to be presented during the first session of the meeting.

Appendix 4: List of current and projected nanotechnology applications in the food and agriculture sectors

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
Nanostructured (also termed nanotextured) food ingredients	Processed nano-structures in food	Novel or improved tastes, flavours, textures	Use of less fat, better tasting food products, more stable emulsions. A typical product of this technology would be in the form of a low-fat nanotextured product (e.g. ice cream, mayonnaise, spread, etc.) that is as "creamy" as the full-fat alternative, and hence would offer a "healthy" option to the consumer.	Ingestion via food/drinks.	Currently, there is no clear example of a proclaimed nanostructured food product that is available commercially, although some products are known to be at different stages of R&D – some may be near market.	One example, currently under R&D, is that of a mayonnaise which is composed of an emulsion that contains nanodroplets of water inside. The mayonnaise would offer taste and texture attributes similar to the full fat equivalent, but with a substantial reduction in the fat intake of the consumer.
Nanodelivery systems for nutrients and supplements	Nano-encapsulated bioactive substances in the form of nanomicelles, liposomes or biopolymer-based carrier systems – mainly additives and supplements for food and beverage	The nanocarrier systems are used for taste masking of ingredients and additives such as fish oils, and protection from degradation during processing.	Preservation of ingredients and additives during processing and storage, masking unpleasant tastes and flavours, controlling the release of additives, as well as enhanced	Ingestion via food/drinks.	A number of delivery systems are available with a range of encapsulated materials, for example, food additives (e.g. benzoic acid, citric acid, ascorbic acid), and food supplements (e.g. vitamins A and E, isoflavones, ß-carotene,	The increased absorption, uptake and improved bioavailability of nutrients and supplements may also have the potential to alter tissue distribution of the substances in the body.

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
	products.	They are also claimed for improved bioavailability of nutrients/ supplements, antimicrobial activity, improved optical appearance, and other health benefits.	uptake of the encapsulated nutrients and supplements.		lutein, omega-3 fatty acids, coenzyme-Q10).	
Organic nanosized additives for food, health food supplements, and animal feed applications	Organic additives (many of them naturally occurring substances) manufactured in the nanosize range.	Due to larger surface area, lower amounts would be needed for a function, or a taste attribute.	The main advantage is claimed to be the better dispersability of water-insoluble additives in foodstuffs without the use of additional fat or surfactants, and enhanced tastes and flavours due to enlarged surface areas of the nano-sized additives compared with conventional bulk forms. Virtually all products in this category are also	Ingestion via food/drinks.	A number of products is available.	This type of application is expected to exploit a much larger segment of the food and health food sector, encompassing colours, preservatives, flavourings, and supplements. A range of products containing nanosized additives is already available in the supplements, nutraceuticals, and food and health food sectors. Examples include vitamins, colorants, flavoring agents, antioxidants, etc.

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
			claimed for enhanced absorption and improved bioavailability in the body compared with conventional equivalents.			
Inorganic nanosized additives for food, health food supplements, and feed applications	Inorganic additives manufactured in the nanosize range	Due to larger surface area, lower amounts would be needed for a function, or taste attribute. Other projected benefits include antimicrobial activity etc.	Enhanced tastes and flavours due to enlarged surface areas of the nanosized additives over conventional forms. Products in this category are also claimed for enhanced absorption and improved bioavailability in the body compared with conventional equivalents.	Ingestion via food/drinks, and potential bioaccumulation in the body.	A range of inorganic additives is available in the supplements, nutraceuticals, and food and health food sectors. These include inorganic materials (including alkaline earth metals, and non-metals, and surface functionalized materials). Examples include silver, iron, silica, titanium dioxide, selenium, calcium, magnesium, etc.	
Food packaging applications	Plastic polymers containing (or coated with) engineered nanomaterials for	Improved mechanical and functional properties of polymers used	"Improved" food contact materials (FCMs) in terms of flexibility, gas barrier properties	Through (potential) migration into foodstuffs, or ingestion of edible coatings.	Examples include plastic polymers with nanoclay as gas barrier, nanosilver and nanozinc oxide for	This area of application constitutes the largest share of the current and short-term predicted market for

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
	improved mechanical or functional properties.	as food contact materials or in food packaging.	and temperature/ moisture stability. "Active" FCMs incorporating metal or metal oxide nanoparticles (e.g. silver, zinc oxide, magnesium oxide) for antimicrobial properties. They are claimed to prevent microbial growth on the surface of plastics and hence keep the food fresher for relatively longer periods.		antimicrobial action, nanotitanium dioxide for UV protection in transparent plastics, nanotitanium nitride for mechanical strength and as a processing aid, nanosilica for surface coating, etc.	nanotechnology applications in the food sector.
Nanocoatings on food contact surfaces	Nanoscale coating.	Nanocoatings for FCMs with barrier or antimicrobial properties.	For "active" or self-cleaning surfaces in food processing facilities such as abattoirs.	Through potential migration into foodstuffs.	A number of nanomaterial-based coatings are available for food preparation surfaces, and for coating food preparation machinery.	Incorporating nanomaterials, e.g. silica or titanium dioxide for self-cleaning surfaces, silver for antimicrobial activity to maintain hygienic environment, or nanoscale lipid structures for water-repellent surfaces.
Surface	The 2nd generation	For food		Through potential	Main uses are currently	Examples include

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
functionalized nanomaterials	nanomaterials that add certain functionality to the matrix, such as antimicrobial activity, or a preservative action, such as through absorption of oxygen.	packaging materials, functionalized ENMs are used to bind with the polymer matrix to offer mechanical strength or a barrier against movement of gases or volatile components (such as flavours) or moisture.		migration into foodstuffs.	in food packaging, possible uses are also emerging in animal feed.	organically modified nanoclays that are currently used in food packaging to enhance gas-barrier properties.
Nanofiltration	Filtration products based on porous silica, regenerated cellulose membranes.	Filtration of undesired components in food – such as bitter taste in some plant extracts. Also clarifying wines and beers.	Potential removal from food of undesirable tastes, flavors, toxins, etc. Removal of insoluble suspended matter from beers and wines.	Ingestion via food/drinks. Potential exposure only if silica remains in the filtered products in free nanoparticulate form.	Colloidal silica (thought to be in micro-sized agglomerated form) is known to be used in clarifying beers and wines.	
Nanosized agrochemicals	Nanosized fertilizers, pesticides, veterinary drugs	Improved delivery of agrochemicals in the field, better efficacy of pesticides, better control over dosing of			Nano-encapsulated and solid lipid nanoparticles have been explored for the delivery of agrochemicals, such as slow- or controlled-release fertilizers and	There is no clear cut example of an available nanoformulated pesticide or other agrochemical compound (e.g. a veterinary medicine). Most examples are for

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
		veterinary products.			pesticides. One reported example is a combined fertilizer and pesticide formulation encapsulated in nanoclay for slow release of growth stimulants and biocontrol agents	products under development that are currently at R&D stage.
Nanosensors for food labeling	Incorporation of nanomaterials into intelligent inks (that respond to a change in the packaged food) to print labels that can indicate the safety and security of the packaged foodstuffs.	Sensors that can monitor condition of the food during transportation and storage.	Better food authenticity, safety and security from the use of "Intelligent" and "Smart" packaging, which incorporate nanosized nanobarcodes, and sensors that can monitor condition of the food during transportation and storage.	Through (potential) migration into foodstuffs.	A few labels are already available. Many others are under development. This area of application is likely to see a rapid growth in the future.	Of particular interest in this regard are the safety and quality indicators that can be applied as labels or coatings to add an intelligent function to food packaging. For example, to monitor the integrity of the packages sealed under vacuum or inert atmosphere by detecting leaks, freeze–thaw–refreeze scenarios by detecting variations in time–temperature, or microbial safety by detecting the deterioration of foodstuffs.
Water decontamination	Nano-iron, other photocatalysts may	Water treatment	Breakdown of organic pollutants,	Treated drinking water, or wastewaters used in	Nano-iron produced and available in large	A number of companies are thought

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
	also be used.		oxidation of heavy metals, elimination of pathogens.	agriculture and food production.	scale quantities.	to be using the technology in developing countries.
Other applications		Animal feed		Through carry-over from consumption of animal products (such as meat, milk). Animal welfare may also be an issue.	Theoretically, any nanosized mineral, vitamin, or other additives and supplements developed for food and health food applications can equally be used for animal feed. .	Some examples of nanosized additives that have specifically been developed (or are under development) for animal feed are available.

Appendix 5: Case studies and illustrative examples

Case Study1: ß-cyclodextrin as a nanocarrier

ß-Cyclodextrin is a cyclic heptamer composed of seven glucose units joined "head-to-tail" by alpha-1,4 links. It is produced by the action of the enzyme cyclodextrin glycosyl transferase (CGT) on hydrolysed starch syrups. CGT is obtained from *Bacillus macerans*, *B. circulans* or related strains of *Bacillus.*

As a result of its cyclic structure, ß-cyclodextrin has the ability to form inclusion compounds with a range of molecules, generally of molecular mass less than 250. Consequently, it is used as a carrier and stabilizer of food flavours, food colours and some vitamins.

Available data demonstrate that ß-cyclodextrin is resistant to metabolism in the upper GI tract but biokinetic studies in rats using radiolabelled ß -cyclodextrin demonstrate that the nanomaterial is readily metabolised in the large intestine to open-chain dextrins/glucose through the combined action of endogenous microflora and amylases.

Available data demonstrate that ß-cyclodextrin is not absorbed to a significant extent from the stomach or small intestine of rats and that excess ß-cyclodextrin is expected to be excreted in faeces. The intestinal absorption, digestibility by the colonic microflora and urinary excretion of ß-cyclodextrin have been studied. Using everted sacs of rat small intestine *in vitro* and ligated gut loops *in vivo,* absorption was shown to be slow, concentration dependent, not saturable and not inhibited by phloretin; this indicates that a passive transport process is involved.

Rat and human caecal microflora were able to utilize ß-cyclodextrin under anaerobic conditions *in vitro,* indicating that the compound is probably hydrolysed to glucose by bacterial enzymes. Based on the above, it is believed that ß-cyclodextrin may be utilized but only indirectly by the activity of the gut flora. Moreover, additional high-dose (>3g/kg bw/day) experiments in the rat demonstrate that only negligible amounts of ß-cyclodextrin remain in the GI tract and over 95% of ingested ß-cyclodextrin is metabolized to glucose in the intestine. Absorption of ß-cyclodextrin was also negligible in a study in beagle dogs and it was shown to be excreted in the urine.

Expected consumer exposure to ß-cyclodextrin was estimated to be between 1.0 and 1.4 mg/kg bw/day from its use as a carrier for flavours, colours and nutrients based on intended use levels in food and data on food consumption patterns. An acceptable daily intake (ADI) of up to 5 mg/kg bw/day of ß-cyclodextrin was estimated from a very large and comprehensive database of toxicity testing. Additional *in vitro* and *in vivo* testing demonsrate that ß-cyclodextrin has little or no potential to affect the absorption of nutrients or to serve as a carrier for unintended substances (JECFA, 1995).

Case Study 2: Zinc oxide as an antimicrobial in food contact material (hypothetical)

The antimicrobial properties of certain metals and metal oxides (e.g. Ag and ZnO) are well known in the literature. The ability of nanotechnology to produce engineered nanoscale metal and metal oxide particles, thereby increasing surface area and potential activity, has increased interest in the use of metals and metal oxides as antimicrobials in food processing and packaging applications. Applications for such materials include as antimicrobials to protect the integrity of packaging or food contact materials or to act as antimicrobials on the food contact surfaces of packaging or food processing equipment.

Some such materials are already commonly found in or added to food or food contact material in their macroscale form. For example, ZnO is used as a nutrient supplement in food and as a colorant and filler in food contact material. The safety of the use of ZnO in a macroscale version is well established.

Exposure to components of food contact materials is typically estimated using experimental migration data or migration modelling or by assuming complete migration to an estimated quantity of food. For applications in materials at the surface interface with food, migration modelling will not typically work well. Moreover, existing migration models will typically incorporate few data on nanoparticles, necessitating that care be applied in their application to the evaluation of nanoscale migrants.

Because of the challenges in analysing migrants in food matrices, migration experiments are typically performed using food simulants. Reactivity of the migrant with the simulant is always a concern but may be more so with nanoscale materials engineered to have a greater surface area and a higher activity. Therefore, in order to address exposure, it may be necessary to determine the form of the nanomaterial entering food. Alternatively, assumptions may be made that any ZnO detected migrating from the food contact material is in the most toxic form. The latter assumption may require additional safety testing data on nanomaterial forms to address a higher estimated exposure.

In cases where a more precise exposure profile may be desired in order to reduce the need for toxicity testing, the identity and physical characteristics of migrants would need to be further analyzed and established. For example, it would be necessary to demonstrate whether the ZnO particle migrates into food and remains suspended as a nanoscale particle, or whether the nanoscale substances are ionized, aggregated or agglomerated in the process of migration or in food. Such information will also be used to determine the applicability of any toxicity data on the macroscale version of the material.

Whether the tested substance is the macroscale version or the nanoscale version of ZnO, the relevance of any planned or existing toxicity test must rely on the relationship of the substance tested to the substance to which consumers are exposed. Toxicity testing recommendations for components of food contact materials are typically tiered based on migration levels or likely consumer exposure. The expectation of greater bioavailability for a nanoscale ZnO will, at a minimum, suggest more intensive testing at a lower level of mass–mass exposure. Alternatively, more sophisticated analysis of exposure or internal dose may be necessary to relate toxicity data on different versions of the substance or to relate tests using different routes of exposure. In addition to relatively straightforward questions regarding internal dose, assessment of nanomaterials needs to consider alternative mechanisms or sites of toxicity resulting from new properties that alter biological transport. It should be possible to address such questions through bridging studies such as ADME studies or modelling. Finally, depending upon the nature of the ZnO migrating into food, it will be necessary to assess the potential for antimicrobial activity of the material in the body.

Appendix 6: Nanotechnology dialogues

Ongoing projects

Dialogue	Country	General information
Nanotechnology Issues Dialogue Group	UK	The Nanotechnology Issues Dialogue Group (NIDG), chaired by Go–Science, is enabling the responsible development of nanotechnologies and coordinating the activities described in the Government's response on nanotechnologies across departments, agencies and research councils. http://www.dius.gov.uk/partner_organisations/office_for_science/science_in_government/key_issues/nanotechnologies/nidg
Forum Nano	Germany	Forum Nano engages in dialogue with politics, the industry and society, and leads the debate on how nanotechnology can be applied in a more beneficial way. Only sustainable nanotechnology solutions will deliver the benefits that society expects to reap from this technology. Forumnano has participated in the development of a number of codes of conduct, e.g. the "Responsible Nano Code". http://forumnano.com/index.asp
EMPA	Switzerland	Nanosafe textiles dialogue Several activities, see for example: http://www.ncb.ch/documents/nanosafe_71116web.pdf http://www.ncb.ch/documents/78833.pdf
		Nanoconvention (EMPA, Switzerland) [Nanotechnologie und ihre Auswirkungen auf Medizin, Wirtschaft, Umwelt und Gesellschaft *Dialog, Diskussionen, Erfahrungsaustausch, Impulse, Denkanstösse, Visionen*] http://www.empa.ch/plugin/template/empa/*/82191
2nd Annual Massachusetts Nanotechnology Workshop. Promoting the Safe Development of Nanotechnology in Massachusetts	USA	This workshop provides a forum for a continuing dialogue with stakeholders from industry, government, research, academia and others on approaches to protecting workers, public health and the environment from exposure to engineered nanoparticles. The focus is on existing Best Practices and Good Current Practices, the opportunities they present to support safe nanotechnology in Massachusetts, and techniques to measure airborne nanoparticle releases in the workplace. http://www.mass.gov/dep/service/outreach/nano_workshop.htm
NISE Nanoscale Informal Science	USA	The US National Science Foundation has supported a US$20 million program over five years (2005–2010) to promote a network of science museums to foster public dialogue on nanotechnology**.** The NISEnet organization

Dialogue	Country	General information
Education Network		coordinates the activities of five science museums to organise a series of exhibitions and public forums (about 3 a year) to inform and engage the public about N&N its related societal and environmental impact. http://www.nisenet.org/
International Dialogue on a global cooperation in nanotechnology	Belgium	http://cordis.europa.eu/nanotechnology/src/intldialogue.htm Third International Dialogue on Responsible Research and Development of Nanotechnology. Brussels, 11–12 March 2008 ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/report_3006.pdf
BASF	Germany	Continuing dialogue with politics: http://www.basf.com/group/corporate/en/function/conversions:/publish/content/sustainability/dialogue/in-dialogue-withpolitics/nanotechnology/images/Nanotechnology_in_dialogue.pdf
Nanotechnologien – Bedeutung für Gesundheit und Umwelt	Switzerland	http://www.ta-swiss.ch/d/them_nano_pfna.html
Series of global dialogues on nanotechnology	Meridian Institute, USA	Global Dialogue on Nanotechnology and the Poor Dialogue Series on Nanotechnology and Federal Regulation International Dialogue on Responsible Research and Development of Nanotechnology. http://www.merid.org/nano/
Centers for nanotechnology in society	USA	Arizona State University: http://cns.asu.edu/ University of California, Santa Barbara: http://www.cns.ucsb.edu/
Evonik/Degussa Dialogue		Degussa fosters dialogue with authorities, consumers, journalists, politicians and environmental protection organizations at special events organized for this purpose. It fosters debate on the risks and benefits of nanotechnology and endeavours to make this technology transparent and to show the general public how this new technology can be beneficial. http://www.degussa-nano.com/nano/en/dialogue/
USDA Public Perception and Acceptance of	USA	The USDA/CSREES has supported three research projects aiming at better understanding of public perception and acceptance of nanotechnology applications to food and agriculture systems. These projects have three distinctly different approaches and objectives:

Dialogue	Country	General information
Nanotechnology for Food and Agiculture		1. Enhance public understanding of nanotechnology and its relevance to food and agriculture through radio cast of expert interviews; 2. Educate the educators (agriculture and rural extension specialists) to equip them with the current knowledge of benefits and concerns of new and potential nanotechnology applications to food and agriculture; 3. Consumer panel study of acceptance of nanotechnology applications to foods.

Completed projects

Dialogue	Country	General information
Nanotechnology Engagement Group (NEG)	UK	The NEG was established in 2005 to document the learning from a series of groundbreaking attempts to involve members of the public in discussions about the development and governance of nanotechnologies. The NEG studied six UK projects that sought to engage members of the public in dialogue about nanotechnologies. Completed in 2007. http://www.involve.org.uk/assets/Publications/Democratic-Technologies.pdf
EU funded specific support actions (FP6): **http://cordis.europa.eu/fp6/projects.htm**	Nano Dialogue	Enhancing dialogue on nanotechnologies and nanosciences in society at the European level: http://cordis.europa.eu/fetch?CALLER=FP6_PROJ&ACTION=D&DOC=1&CAT=PROJ&QUERY=01213f372fd0:13f7:29534e4f&RCN=74979
	Nanologue	Facilitating the dialogue between research, business and the civil society to improve the quality of life, create wealth and reduce impacts to society: http://cordis.europa.eu/fetch?CALLER=FP6_PROJ&ACTION=D&DOC=3&CAT=PROJ&QUERY=01213f372fd0:13f7:29534e4f&RCN=74431
"Nano-Dialog 2006–2008"	Germany	http://www.bmu.de/english/nanotechnology/nanodialog/doc/40549.php http://bundesumweltministerium.de/gesundheit_und_umwelt/nanotechnologie/nanodialog/doc/37262.php
The Nanodialogues	Sciencewise/ Demos/ Lancaster University, UK	http://www.demos.co.uk/files/Nanodialogues%20-%20%20web.pdf?1240939425
Mapping study on regulation and governance of nanotechnologies. FramingNano Project		A multi-stakeholder dialogue platform framing the responsible development of nanosciences and nanotechnologies www.framingnano.eu

Dialogue	Country	General information
Comparative Challenge of NANOmaterials (CONANO Dialogue)	Switzerland, Austria, Germany	http://www.ecology.at/files/berichte/E11.565.pdf http://www.ecology.at/conano_dialog.htm
Small talk	UK	The project looked at the benefits for the science communication community in working together on dialogue activities for an "upstream" issue – nanotechnology. This report presents the findings of this project for both science communicators and policy-makers: http://www.smalltalk.org.uk/page41g.html
Nano Risk Framework (DuPont and Environmental Defense Fund)		http://www.nanoriskframework.com/page.cfm?tagID=1095
Dialogue on Nanoparticles	Germany	http://www.dialog-nanopartikel.de/downloads_en.html
NanoJury	UK	http://www.nanojury.org.uk/index.html

Appendix 7: Topics and processes for nanotechnology dialogues

To / From	Public Authorities	Industry	Academia	Society (incl. elected representatives, NGOs)	Media
Public Authorities	Content: RA, guidance, regulation Process: formal (official journal publications, EU comitology, etc.), informal (hearings, conferences, etc.)	Content: safety assessments, market developments Process: formal (submissions for authorization); informal (conferences, hearings, mailings, etc.)	Content: risk assessement, science Process: evaluations, scientific opinions, journal publications, conferences	Content: public opinion, societal issues (consumer/environmental protection and safety) Process: public consultations, conferences, public hearings, mailings, public surveys	Content: market, regulatory and legal, national and international developments, public opinion Process: scientific publications, articles/reportages, coverage of conferences, public consultations and hearings
Industry	Content: legal requirements, safety assessment guidelines Process: formal (official journal publications, EU comitology, etc.), informal (hearings, conferences, etc.)	Content: safety assessments, technological and market developments, regulatory developments Process: open conferences, closed corporate workshops, industry association meetings, etc.	Content: science Process: scientific advice, journal publications, conferences, workshops	Content: public opinion, societal issues (consumer/environmental protection and safety) Process: participation at open conference/forums, science fairs and workshops where industry presents products/developments; industry's consumer information services	Content: Process:
Academia	Content: RA, guidance, regulation, calls for proposals Process: formal	Content: safety assessments, market developments Process: formal (safety	Content: science, risk assessment Process: conferences, scientific journals,	Content: public opinion, ethical/safety concerns, Process: open conferences/forums,	Content: Process:

	(official journal publications, etc.), informal (hearings, conferences, etc.)	"dossiers", when scientists serves as risk assessors for public authorities, journal publications, professional publications); informal (conferences)	workshops	science fairs and workshops	
Society (incl. elected representatives, NGOs)	Content: RA, guidance, regulation Process:	Content: Safety assessments, market developments Process: conferences, workshops, hearings, mailings, etc.; science fairs and workshops, consumer information services	Content: science Process: Open conferences/forums, science fairs and workshops.	Content: Process:	Content: Process:
Media	Content: science, economics, policy, RA, guidance, regulation Process: formal (press conferences, press releases, etc.); informal (speeches, presentations, interviews)	Content: market development, Process: formal (press conferences, press releases, etc.); informal (speeches, presentations, interviews, products advertisement/promotion)	Content: scientific and technological developments Process: scientific opinions, journal publications, conferences, press releases	Content: public opinion Process: speeches, presentations, interviews, public surveys	Content: Process: