State of the art on the initiatives and activities relevant to risk assessment and risk management of nanotechnologies in the food and agriculture sectors

FAO/WHO technical paper

World Health Organization

Food and Agriculture Organization of the United Nations

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Abbreviations and acronyms

ABDI	Brazilian Agency for Industrial Development
ADI	Acceptable Daily Intake
AFC	(former) Panel on food additives, flavourings, processing aids and materials in contact with food, EFSA (replaced by two separate Panels, ANS and CEF, in 2008)
ANEC	European Consumer Voice in Standardisation
ANS	Panel on food additives and nutrient sources added to food, EFSA
BEUC	Bureau Européen des Unions de Consommateurs (European Consumers' Organisation)
BSI	British Standards Institution
CEF	Panel on food contact materials, enzymes, flavourings and processing aids, EFSA
DNA	Deoxyribonucleic acid
EC	European Commission
EFSA	European Food Safety Authority
ENM	Engineered nanomaterials
EPA	United States Environmental Protection Agency
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FDA	United States Food and Drug Administration
FSANZ	Food Standards Australia New Zealand
FSCJ	Food Safety Commission, Japan
IFT	Institute of Food Technologists
IG DHS	Interessengemeinschaft Detailhandel Schweiz
ILSI	International Life Sciences Institute
ISO	International Organization for Standardization
JECFA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	Joint FAO/WHO Expert Meeting on Pesticide Residues
JRC	Joint Research Centre, European Commission
MINChar	Minimum Information on Nanoparticle Characterization

MRC	Medical Research Council, UK
NEHI	Nanotechnology Environmental and Health Implications (working group of the NSET Subcommittee)
NIA	Nanotechnology Industries Association
nm	Nanometre
NRC	National Research Council, USA
NRP	National Reserch Programme, Switzerland
NSET	Nanoscale Science, Engineering, and Technology
OECD	Organisation for Economic Co-operation and Development
SCCS	Scientific Committee on Consumer Safety, European Commission
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks, European Commission
SECO	State Secretariat for Economic Affairs, Switzerland
UV	Ultraviolet
WHO	World Health Organization

State of the art on the initiatives and activities relevant to risk assessment and risk management of nanotechnologies in the food and agriculture sectors

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1. Background

An international expert meeting on the potential food safety implications of the application of nanotechnologies in the food and agriculture sectors was convened by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) in June 2009. The key findings, conclusions and recommendations of the meeting were published in 2010 (FAO/WHO, 2010) and are briefly summarized in section 1.2 below.

1.1 Methodology

This report was commissioned by FAO and WHO with the objective of summarizing and analysing the information that has become available since the 2009 expert meeting and determining possible courses of action to be followed by FAO and WHO in this matter.

Following up on one of the recommendations of the 2009 FAO/WHO expert meeting, the present report reviews national and international activities on the risk analysis of nanomaterials in the food and agriculture sectors that have been carried out since the meeting. It presents national and international risk assessment and risk management approaches that identify and implement strategies to address potential hazards associated with the use of nanotechnology-related products or techniques.

Information on relevant regulations and risk assessment activities was gathered from the web sites of national and international institutions, organizations and governments. Those had been identified due to contributions made to the 2009 experts meeting and by searching the internet for keywords such as “nanomaterial”, “food”, “regulation”, and “safety”. Specific reference to these web sites is given in the respective sections of this report. It should be noted that terms used in this report reflect the definitions applied within the various sources of information; no attempt was made to align the terminology with definitions agreed to by the 2009 expert meeting or other definitions applied internationally – for example, by the Codex Alimentarius Commission.

Information on actual and planned uses of nanomaterials resulting in human exposure through food or food packaging/contact materials since 2009 was collected from a variety of sources, including the scientific literature, web sites, patent databases, market analysis reports and material presented at conferences, workshops and symposia.

The draft report was circulated to Codex members and observers and other interested parties in June 2012 for a public review. Comments received until end of November were considered and the report was amended as appropriate.

1.2 Summary of the FAO/WHO expert meeting in 2009

Use of nanotechnology

The expert meeting agreed that nanotechnology offers considerable opportunities for the development of innovative products and applications for agriculture, water treatment and food production, processing, preservation and packaging, and its use may benefit farmers, the food industry and consumers alike. It was noted that nanotechnology-derived food products will be increasingly available to consumers worldwide.

It was recognized that there was a need for clear and internationally recognized definitions and that gaps in definitions in the food area could be addressed by the Codex Alimentarius Commission.

Assessment of human health risks

Materials that are produced intentionally with structural features at a nanoscale range (between 1 and 100 nm) may have properties that are different from those of their conventional counterparts. Such differences may have an impact on human health following consumer exposure to nanomaterials.

Current risk assessment approaches used by FAO, WHO and the Codex Alimentarius Commission were considered to be suitable for engineered nanomaterials used in food and agriculture. Additional safety concerns may arise owing to the characteristic properties of nanomaterials that make them different from their microscale/macroscale counterparts. For example, the very high surface area of engineered nanomaterials has consequences that need to be considered in their risk assessment. Nanoparticles may interact with other substances present in the food matrix, and such effects and interactions of engineered nanomaterials need to be characterized. Understanding their fate in the environment is also important, as it may result in indirect human exposure.

The experts agreed that risk assessment strategies might benefit from the use of a tiered approach for prioritization of the types or classes of material for which additional data are likely to be necessary to reduce uncertainties in the risk assessment. Further research could lead to novel risk assessment strategies; the development of validated testing methods and guidance would help to address specific data gaps.

Stakeholder confidence and dialogue

Engagement of stakeholders was acknowledged as imperative for any emerging or controversial issue in the area of food safety. Critical to the success of a research strategy for nanomaterials would be addressing the key interests, priorities and concerns of stakeholders and ensuring that all potential pathways and risks are addressed.

Consumer attitudes towards the application of nanotechnology in food and agriculture were seen as complex; consumer understanding of the potential risks and clear, tangible benefits of nanotechnology was key. It was noted that advocacy groups had expressed the desire for industry and governments to implement measures to protect consumers from the consequences of the unregulated release of commercial nanoproducts.

Greater access of scientists to the public debate was needed. A forum for continued international dialogue to develop strategies to address stakeholder issues was proposed, and it was noted that the public should be engaged at the national level. Also, the existing FAO/WHO food safety risk analysis framework might be reviewed in particular with regard to engaging stakeholders. Mechanisms should be identified to support the need for transparency and traceability of nano-enabled products or engineered nanomaterials in food and agriculture and their associated risks.

2. Application of nanomaterials in food: current status

Food can be cultivated, produced, processed or packaged with nanotechnology, or engineered nanomaterials can be added to food. The list of current and projected nanotechnology applications in the food and agriculture sectors in Appendix 4 of the report from the FAO/WHO expert meeting (FAO/WHO, 2010) was found to be accurate and up to date.

Within the period 2009–2011, 183 patents were published that contain the keywords "nano* AND food*" in the patent title (http://wokinfo.com/, accessed 2 January 2012). Among these patents, 47 related to packaging or coating applications. Furthermore, 19 patents concerned nano-additives, and 10 patents covered nanotechnology applications for the detection of compounds in food.

Examples of potential uses of nanomaterials in food and beverages, for food storage and for food preparation on the United States market can be found on the web site of the Project on Emerging Nanotechnologies of the Woodrow Wilson International Center for Scholars (http://www.nanotechproject.org/). A report from the European Consumer Voice in Standardisation and the European Consumers' Organisation contains several lists of consumer products, among them food supplements, that claim to contain nanomaterials (ANEC/BEUC, 2009).

The use of nanotechnology and nanomaterials in food and agriculture was also the focus of a number of review monographs that summarize the status quo or state of art (Chaudry *et al.*, 2010; Frewer *et al.*, 2011; Huang, 2012).

In general, more research on the application of nanomaterials in food is expected. In particular, research on nanoemulsion will increase because of the transfer from parallel efforts in the drug delivery sector (ObservatoryNANO, 2010). However, there are some barriers to commercialization for nanoemulsions. First, suitable food-grade ingredients must be identified for formulating food nanoemulsions. Second, many of the approaches that have been developed within research laboratories may not be suitable for scale-up to industrial production; suitable processing operations must be identified for economic production of food-grade nanoemulsions on an industrial scale. Third, as nanodroplets may have an enhanced bioavailability, in vivo evaluation of nanoemulsion droplets is required; however, such studies are limited (McClements & Jiajia, 2011).

With respect to the use of nanotechnology, it is important to consider all areas potentially associated with food safety; such areas may to a certain extent go beyond the borders of traditional activities.

One specific area of interest is the use of nanomaterials in wastewater treatment to improve the quality and safety of water used for agriculture, aquaculture and human consumption. It might be possible to develop, for example, low-cost nanofilter/nanomembrane materials that could be of interest to developing countries. However, such new materials and uses may pose safety issues not related to food safety, such as their disposal at the end of their life cycle (FAO/WHO, 2012).

For animal health, the development of so-called "nanovaccines" with improved delivery routes to target animals of small size in aquaculture (e.g. fish larvae, shrimp) could be of benefit from a cost and animal welfare point of view. However, research seems to be in an early conceptual stage; no information is available on already ongoing technical projects (FAO/WHO, 2012). Testing kits to identify animal or zoonotic pathogens and nanoscale drug delivery routes have been identified as application areas of potential benefit for animal husbandry in developing countries (FAO/WHO, 2012).

Technological solutions using nanotechnology in packaging to reduce food losses or facilitate traceability could be of interest (FAO/WHO, 2012).

The future use of nanomaterials, especially for industrial purposes, has recently raised specific concerns regarding their disposal at the end of their life cycle. Such materials may not be degradable and may persist in the environment where they may interact with compounds in the environment. This potential hazard is already causing concern in developing countries to which waste containing nanomaterials may be exported (FAO/WHO, 2012).

3. Relevant activities at the national/regional level since 2009

This section briefly summarizes national and regional initiatives and activities related to the risk assessment and risk management of nanomaterials, such as research projects, development of guidance documents and drafting of regulations, that have been carried out since the FAO/WHO expert meeting in 2009. Emphasis is placed on issues that contribute to the definition of the term "nanomaterials" (to be subjected to specific risk assessments) and case-studies where a risk assessment has been undertaken for a defined material.

One needs to keep in mind that these national and regional initiatives were not undertaken in a regulatory or scientific vacuum. The countries concerned usually have regulatory frameworks in place that deal with food safety and consumer protection, such as risk assessments for food chemicals, product labelling and market access authorization. The absence of legislation dealing specifically with nanomaterials used in foods does not mean that such products fall into a regulatory gap. Modern food legislation regulates many issues related to, for example, consumer health, consumers' right to information, fair trade practices and the environment, many of which may be applied to nanotechnology and nanomaterials used in foods.

3.1 Australia/New Zealand

Risk management

All food supplied in Australia and New Zealand must comply with the Australia New Zealand Food Standards Code and be safe for human consumption. Any new food substances manufactured using nanotechnologies that may present safety concerns will have to undergo a comprehensive scientific safety assessment under the appropriate standard before they can be legally supplied in Australia and New Zealand (FSANZ, 2011).

Food Standards Australia New Zealand (FSANZ) recently published an article describing its regulatory approach to nanoscale materials in the *International Food Risk Analysis Journal* (Fletcher & Bartholomaeus, 2011). The primary focus is not on the size of the material per se, but on materials likely to exhibit physicochemical and/or biological novelty. FSANZ differentiates between nanoscale materials that undergo dissolution in water or oil in the final food or in the gastrointestinal tract and nanoscale or microscale

materials that are insoluble in water and oil and non-biodegradable, particularly those that may not be readily excreted. The latter type of material may require additional regulatory examination due to its particulate nature.

Risk assessment

FSANZ has not yet received any applications to approve any novel type of engineered nanoscale particles for food use. Therefore, no risk assessments have been undertaken.

3.2 Brazil

On 9 August 2011, experts from the Brazilian Competitiveness Forum on Nanotechnology met in São Paulo to address the issue of regulating nanotechnology for the industrial sector (NIA, 2011). The meeting was attended by representatives of the working groups of the forum, who discussed a study funded by the Brazilian Agency for Industrial Development on the development of possible standards, laws and guidelines for nanotechnology regulation in Brazil (ABDI, 2010).

3.3 Canada

Risk management

Regulations in Canada make no explicit reference to nanomaterial at this time. Health Canada helps protect and promote health by using existing legislative and regulatory frameworks to mitigate the potential health risks of nanomaterials and to help realize their health benefits.

Health Canada considers any manufactured substance or product and any component material, ingredient, device or structure to be a nanomaterial if it is at or within the nanoscale in at least one external dimension or has internal or surface structure at the nanoscale; or it is smaller or larger than the nanoscale in all dimensions and exhibits one or more nanoscale properties/phenomena (Health Canada, 2011).

Health Canada encourages stakeholders to communicate with the responsible regulatory authority early in the development process, especially for combination products that are, contain or make use of nanomaterials. In order to identify and assess potential risks and benefits of nanotechnology-based health and food products, Health Canada encourages manufacturers to request a pre-submission meeting with the responsible regulatory authority to discuss the type of information that may be required for their product's safety assessment.

3.4 China

Risk management

In China, a general Food Safety Law came into effect on 1 June 2009 (Food Safety Law of China, 2009). According to this law, risk assessment has to be conducted by the Ministry of Agriculture and the Ministry of Health (Articles 4–17) (Poto, 2011). The law

will enhance monitoring and supervision and strengthen safety standards (Qian *et al.*, 2011). The law does not contain any legislation relating to nanomaterials (Food Safety Law of China, 2009). Until now, applications for using nanominerals or food ingredients have been rejected by regulatory authorities, but the safety evaluation of nanotechnology in foods continues to be discussed.

3.5 European Union

Risk management

Regarding the definition of nanomaterials, the Scientific Committee on Emerging and Newly Identified Health Risks published the opinion "Scientific basis for the definition of the term nanomaterial" in 2010 (SCENIHR, 2010). Based on this, the European Commission adopted the following recommendation on the definition of nanomaterial in 2011 (EC, 2011):

> "Nanomaterial" means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm–100 nm."

The European Commission recommends that this definition, which is complemented by further definitions for terms used, such as aggregate, be used as a reference to determine whether a material is considered as a nanomaterial for legislative and policy purposes in the European Union.

The European Union action plan on nanotechnologies for the next few years is currently under preparation. Results from the public consultation launched to support the preparation of the new action plan are available in a summary paper (EC, 2010). Responses were received from the general public, individual researchers, research organizations, industry, public authorities and nongovernmental organizations.

Very recently adopted new legislation that regulates food information also addresses the presence of engineered nanomaterials in foods (EU, 2011). Article 18 of Regulation (EU) No. 1169/2011 states that "All ingredients present in the form of engineered nanomaterials shall be clearly indicated in the list of ingredients. The names of such ingredients shall be followed by the word 'nano' in brackets" (EU, 2011). This regulation is going to apply from 13 December 2014. It also provides, for food, a legal definition of an "engineered nanomaterial", which

> "…means any intentionally produced material that has one or more dimensions of the order of 100 nm or less or that is composed of discrete functional parts, either internally or at the surface, many of which have one or more dimensions of the order of 100 nm or less, including structures, agglomerates or aggregates, which may have a size above the order of 100 nm but retain properties that are characteristic of the nanoscale."

Properties that are characteristic of the nanoscale include (1) those related to the large specific surface area of the materials considered and/or (2) specific physicochemical

properties that are different from those of the non-nanoform of the same material. The regulation foresees adjustments to the definition in view of technical and scientific progress, or a definition agreed at international level.

A common system for authorisation of food additives is in place in Europe since 2010 which requires re-evaluation of the safety of any food additive to ensure that, once permitted, food additives are kept under continuous observation and re-evaluation. This shall assure that an approved additive produced by a different production process (e.g. to generate nano-form) will undergo re-evaluation of safety.

An up-to-date overview of European policies for nanomaterials in food and feed with a focus on comparing lessons learnt from the regulatory approach to genetically modified organisms was completed recently by Bucatariu (2011). The author argues that a coherent approach to ensuring the safety and security of food and consumers in the European Union should also support active and responsible involvement in the global perspective (e.g. trade, innovation, sustainability) along with European Union research and development funding and partnerships.

Risk assessment

In 2011, the European Food Safety Authority (EFSA) published a scientific opinion with the title "Guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain" (EFSA Scientific Committee, 2011). The guidance is a practical approach to assessing potential risks when nanomaterials are applied in the food and feed chain. It builds upon the scientific opinion from 2009 (EFSA, 2009).

EFSA concluded in both reports that "the risk assessment paradigm (hazard identification and hazard characterisation followed by exposure assessment and risk characterisation) is appropriate for these applications" of nanoscience and nanotechnologies in the food and feed chain.

Therefore, the risk of an engineered nanomaterial will be determined by its chemical composition, physicochemical properties, interactions with tissues and potential exposure levels. EFSA states that there are currently uncertainties related to the identification, characterization and detection of engineered nanomaterial because of the lack of suitable and validated test methods. For these reasons, EFSA recommends that additional research is needed to address the many current uncertainties and limitations. In general, EFSA supports the use of conventional risk assessment while acknowledging the limited knowledge on exposure to nanofood applications.

Opinions on four nanomaterials from two EFSA panels have been published so far (L. Djien, EFSA, personal communication, 2011). For silicon dioxide coating (maximum thickness 100 nm) on the inner surface of polyethylene terephthalate articles, the Panel determined that the tested substance was not genotoxic (AFC, 2007). Regarding nanoparticles of titanium nitride used in polyethylene terephthalate bottles at concentrations up to 20 mg/kg, the Panel considered that the intended use of this substance would not give rise to exposure via food and hence was not of toxicological concern (CEF, 2008). For the nanoparticle silver hydrosol, the Panel concluded that due

to the lack of an appropriate dossier supporting its use, its safety and the bioavailability of silver from silver hydrosol could not be assessed (ANS, 2008). For calcium carbonate, the Panel noted that the presence of unintentional nanoscale particles at trace levels in food additive grade calcium carbonate could not be excluded. While the data were inadequate to reach definitive conclusions on calcium carbonate predominantly in the nanoscale, the Panel concluded that the available data were sufficient to conclude that the current levels of adventitious nanoscale material within microscale calcium carbonate would not be of additional toxicological concern (ANS, 2011).

The EFSA has set up a scientific network on the risk assessment of nanotechnology in food and feed, in which all member states are represented. This network aims to create an overview of national research activities to facilitate collaboration and exchange of information [http://www.efsa.europa.eu/en/supporting/pub/362e.htm].

Although not food related, it is of interest to note that risk assessments are ongoing on three specific manufactured nanomaterials (ultraviolet filters) for authorization of their use in cosmetics.

Although not food related, it is of interest to note that the first regulatory risk assessments have recently been carried out on manufactured nanomaterials for their intended use as ultraviolet filters in cosmetic products. These include opinions on a nano-scale organic UV filter (SCCS 2011), and nano-forms of zinc oxide (SCCS 2012a).

In June 2012, the European Commission's Scientific Committee on Consumer Safety published guidance on the safety assessment of manufactured nanomaterial in cosmetic products (SCCS, 2012b).

Research on nanomaterials

The FAO/WHO expert meeting in 2009 called for innovative and interdisciplinary research that may lead to novel risk assessment strategies for the application of nanotechnologies in food and feed. Several corresponding research projects on nanomaterials were funded by the European Union's framework programmes for research and technological development. Ongoing and finished projects related to nanotechnology are provided on the European Commission's web site on nanotechnology (http://cordis.europa.eu/nanotechnology/home.html).

One of these projects, called NanoLyse, focuses on nanoparticles in food and is dedicated to the development of analytical methods for the detection and characterization of engineered nanoparticles in food. The NanoLyse consortium comprises 10 universities and research centres from Europe and Canada. The project started in January 2010 and will last for three years (NanoLyse, 2011). According to NanoLyse, very limited knowledge is available on the potential impact of engineered nanoparticles on consumers' health. The NanoLyse project will develop a toolbox of methods to detect and characterize different types of engineered nanoparticles in food. Recent project outcomes have been presented in several scientific publications (Allmaier *et al.*, 2011; Dudkiewicz *et al.*, 2011; Linsinger *et al.*, 2011; Peters *et al.*, 2011; Von der Kammer *et al.*, 2011).

Another project funded by the European Union's framework programme is ObservatoryNANO. The project is led by the United Kingdom's Institute of Nanotechnology; it has as a final goal the establishment of a permanent European Observatory on Nanotechnologies. ObservatoryNANO publishes factsheets that provide information on nanotechnology developments in different sectors, including the agrifood sector (ObservatoryNANO, 2010, 2011).

The Joint Research Centre of the European Commission maintains a repository of nanomaterials (Gilliland, 2012). These reference nanomaterials enable the accurate comparison of data obtained in different test laboratories worldwide. The 25 types of material include silver nanoparticles, silicon dioxide and titanium dioxide (JRC, 2011).

3.6 Indonesia

No safety assessments or regulations specific to nanomaterials in the food and agriculture sectors were found on the Indonesian government's web site (http://www.indonesia.go.id/en.html) or on a cooperative web site between the private sector and the research community (http://www.nano.or.id/).

3.7 Japan

Risk management

Nanotechnology was specified as one of the priority research targets in the third *Science and Technology Basic Plan* for 2006–2010 by the Japanese government (Government of Japan Council for Science and Technology Policy, 2006). In response to this plan, the Japanese Ministry of Agriculture, Forestry and Fisheries (2007) funded the research project "Food nanotechnology project" in 2007. Scientific papers published under this project evaluate and analyse nanoscale food products.

The Japanese Ministry of Health, Labour, and Welfare launched a six-year programme (2009–2014) called the "Research project on the potential hazards, etc. of nanomaterials", which focuses on the carcinogenicity of nanomaterials. The Japanese Ministry of Economy, Trade and Industry published the results of voluntary information gathering on industry activities on its web site in March 2010 (only in Japanese) (OECD, 2010a).

The fourth *Science and Technology Basic Policy Report*, published in October 2010, stated that the government will promote research and development into nanotechnology (Government of Japan Council for Science and Technology Policy, 2010). In December 2010, the Japanese Center for Research and Development Strategy published a nanotechnology report (Japan Science and Technology Agency, 2010). According to this report, the annual investment in nanotechnology in the United States, China and the Republic of Korea has exceeded that of Japan (Japan Science and Technology Agency, 2010).

Risk assessment

A survey report on the use of nanotechnology in the food sector in March 2010 (FSCJ,

2010), funded by the Food Safety Commission Japan (FSCJ). From the replies to the questionnaire by the domestic industry on the use of engineered nanomaterial, it was concluded that there was no need for specific nanomaterial regulation at present. However, the report also concluded that there were questions on the classification of nanotechnology-using food products as well as significant data gaps, which precluded the drawing of firm conclusions. If any regulation needed to be introduced, safety assessment methods would need to be established first.

3.8 Malaysia

Risk management

Nanotechnology has been identified by the National Innovation Council in 2009 as an essential element to meet the country's objective to turn Malaysia into a high income developed nation by 2020. In 2010 the national Nanotechnology Directorate established under the Ministry of Science, Technology and Innovation launched the Nano Malaysia Programme which incorporates various nanotechnology initiatives. The National Nanotechnology Policy and Strategy adopted in 2012 highlights the central role nanotechnology will play and one of the key economic clusters identified is food and agriculture. Nanotechnology shall help to increase agricultural productivity, address pest-resistance and improve food quality. Considering the global outlook in the food and agriculture sector, the application of nanotechnology may improve significantly food security.

In 2011, the Nanotechnology Directorate called for strategic innovative and interdisciplinary research that is in line with the national nanotechnology roadmap. Of the total of 20 projects a number are related to agriculture and food sector.

Under the National Nanotechnology Directorate a Working Committee specifically focussing on issues related to health, safety and environment was established. Such issues are expected to be raised with regards to the use of nanomaterials; industry players and personnel need to be trained, certified and monitored to ensure that safety and health issues are comprehensively addressed. A comprehensive Health, Safety and Environment Management Framework is planned and communicated in a sustained manner through formal studies.

Legal instruments, appropriate parameters and monitoring mechanisms shall ensure compliance with all aspects of nanotechnology development and commercialization. Malaysia is formulating a clear roadmap to comply with any future global safety standards relevant to nanotechnology.

Risk assessment

At present there are no specific regulations applicable to the risk assessment of nanotechnology. All food imported or produced domestically including those containing nanoscale particles, must comply with the Food Act 1983 and related regulations, and must be safe for human consumption. In addition, risk assessment is conducted to address potential health risks and is not limited to nanotechnology.

3.9 Mexico

No safety assessments or regulations specific to nanomaterials in the food and agriculture sectors were found on government web sites relating to food and agriculture: the Mexican Ministry of Agriculture, Livestock, Rural Development, Fisheries and Food (http://www.sagarpa.gob.mx/) and the Mexican National Institute of Public Health (http://www.insp.mx/).

3.10 Republic of Korea

No regulations relating to nanomaterials were found on government web sites: the official web site of the Republic of Korea (http://www.korea.net/index.html), the Korean Ministry for Food, Agriculture, Forestry and Fisheries (http://english.mest.go.kr/web/40724/en/board/enlist.do?bbsId=276) and the Korean Ministry of Education, Science and Technology (http://english.mest.go.kr/enMain.do).

The 3rd International Nanomaterials Ethics Workshop, a gathering of international experts in nanotechnology and science ethics, was held on 14 January 2011 in the Republic of Korea. Topics included changes in safety regulation regarding nanomaterials in European countries. Companies' responses and strategies with respect to the launch and export of nanotechnology products were discussed at the workshop (Korean Ministry of Education, Science and Technology, 2011).

The Korean Ministry of the Environment developed a document on the *Guideline for the life cycle assessment (LCA) of nanomaterials*, as reported in OECD (2011b).

3.11 Russian Federation

Risk management

The control of nanomaterials in various industry sectors, including food and agricultural production receive attention by the Federal Service for Surveillance of Consumer Rights Protection and Human Well-Being (Rospotrebnadzor) since 2007. The Regulation of the Chief State Health Officer of the Russian Federation dated July 23, 2007 N 54 "On supervision of produce, received with use of nanotechnologies and containing nanomaterials" sets several tasks, among them the following:

- to organize the state-wide registration of potentially dangerous nanoparticles and nanomaterials;
- to develop a concept for the supervision of industry sectors using nanotechnologies;
- to inform the population impartially about the use of nanotechnologies and nanomaterials;
- to recommend to industry what data about the use of nanotechnologies or nanomaterials in the manufacturing process they should commnicate in their consumers' information;
- to consider the data on the use of nanotechnologies or nanomaterials when carrying out sanitary and epidemiologic examination of a product.

Several federal ministries and scientific bodies developed "The concept of toxicological researches, methodology of risk assessment, methods of identification and quantitative determination of nanomaterials" (No. 79, 31.10. 2007) which notes that "the set of the stated factors testifies to nanomaterials possessing physical and chemical properties and biological (including toxic) action, differing from substances in a usual physical and chemical condition. In this connection they have to be referred in all cases to new types of materials and production, which characteristic of potential risk for human health and environment is compulsory in all cases".

Risk assessment

Under the umbrella of a federal programm that aimed at the development of infrastructure of Nanoindustry in the Russian Federation for 2008-2010, in total 50 standard and methods documents (guidelines and recommendations) for safety assessment, as well as risk evaluation of the nanotechnologies and nanomaterials were developed and approved by under the auspieces of the Chief State Health Officer of the Russian Federation.

A predictive assessment allows to classify nanomaterials as having high, average or low level of potential hazard. It allows further to determine the necessary tests of nanomaterials on biological objects, such as cultures of microorganisms, aquatic organisms, and laboratory animals. Seventeen documents were developed and put into operation, which consider questions of control and an assessment of risks of the nanomaterials applied in food sector. Special recommendations for methods and guidelines establish sampling of food products and agricultural production, that may contain nanoparticles or come in contact with nanotechnologies. This work is supported by a research reference laboratory that develops analytical methods for the assessment of nanomaterials' and nanoparticles' content in agriculture produce, foodstuff and packaging materials.

The risk evaluation of nanoparticles and nanomaterials in the food sector is based on the traditional scheme which was developed and approved for the assessment of chemical and other technological hazards. This scheme includes: a) identification of a hazard using monitoring data obtained from a product register of potentially dangerous nanoparticles and nanomaterials, surveilllance of use, and forecasts of production for a 5-years period); b) hazard characterization on the basis of the experiments in biological models (laboratory animals) which are carried out in accordance with guidelines and recommendations generally harmonized with requirements of OECD, EFSA, FAO/WHO and other international and national blodies; c) evaluation of exposure on the basis state statistical data and the medico-demographic analysis; d) risk characterization by using, at this stage, a threshold model resulting in a safe reference levels of nanoparticles' impact on the human body. Such reference levels were developed and implemented in sanitary regulations for nanoparticles of silver, single wall carbon nanotubes and titanium dioxide nanoparticles.

As of 2012 safety assessment of a number of nanomaterials used in production of food and agricultural designation were carried out by the "Institute of Nutrition"

of the Russian Academy of Medical Science, in experiments on laboratory. Results for the animals receiving nanomaterials, are compared to data for the relevant control groups of animals who receive not only the carrier (the dispersing medium) of nanoparticles, but also their chemical analog in traditional (not-nano) form. It allows to allocate possible toxic effects of nanoparticles against the influences rendered by the carrier or by a chemical being part of nanoparticles irrespective of degree of its dispersion. Until now such work allowed to characterise nanoparticles of titanium dioxides, silicon, aluminum and iron, the nanostructured clays (nanoexfoliated clay), fulleren C60, metal silver. The results of researches will allow to prove safe levels of action of these nanomaterials at their intake with food or through oral way of exposition. (Tutelyan, 201X).

3.12 South Africa

No safety assessments or regulations specific to nanomaterials in the food and agriculture sectors were found on the Government of the Republic of South Africa's web site (http://www.info.gov.za/view/DynamicAction?pageid=528). *The Foodstuffs, Cosmetics and Disinfectants Amendment Act, 2007* contains no regulations on nanomaterials (Government of the Republic of South Africa, 2008).

South Africa's national nanotechnology strategy runs until 2014. The main objective of this strategy is to support long-term nanoscience research (Department of Science and Technology of the Republic of South Africa, 2011).

3.13 Switzerland

Risk management

The Swiss Federal Council launched the "Action Plan for Synthetic Nanomaterials" that illustrates the work required for the safe handling of nanomaterials in April 2008 which serves as a framework until 2015. The plan addresses development of regulatory framework conditions for the responsible handling of synthetic nanomaterials, creation of scientific and methodical tools aimed at identifying and preventing potential harmful effects of synthetic nanomaterials on health and the environment, and the promotion of the public dialogue on opportunities and risks of nanotechnology.

A number of projects have been implemented within the scope of the Action Plan or by trade organi-sations, the following are of immediate relevance to food safety aspects of nanomaterials:

"The Federal Office of Public Health (FOPH) and the Federal Office for the Environment (FOEN) published a precautionary matrix to assist authorities, industry, trade, commerce and research laboratories in the preliminary clarification of any need for action. The evaluation tool is based on a limited number of evaluation parameters, including size of the particles, their re-activity and their release potential. The matrix applies to nanomaterials smaller than 500 nm (Höck *et al.* 2011).

The Code of Conduct has been drawn up by the Swiss retailer's association IG DHS in order to take account of the growing importance of nanotechnologies in consumer products. Only those products which, according to the latest scientific and technical findings, are considered to be harmless to humans, animals and the environment during manufacture and correct use, may be included in the product range (IG DHS, 2011). For food products the use of the guidance published by the European Food Safety Authority is recommended (EFSA Scientific Committee, 2011)."

Other outputs are not directly related to food but may be of relevance such as a guideline for safety data sheets for synthetic nanomaterials (SECO, 2012), an implementation aid describing the basic principles of the environmentally compatible and safe disposal of this type of waste (FOEN, 2010).

In 2009, the Federal Office of Public Health (FOPH) extended an invitation to initiate a dia-logue with representatives of the authorities, consumer organisations, industry and retail. The purpose was to find ways of informing the public about nanotechnology and its applications in a transparent and easy-to-understand fashion (FOPH, 2010).

The National Research Programme "Opportunities and Risks of Nanomaterials" (NRP 64) aims to bridge the gaps in our current knowledge on nanomaterials. The research projects have started in December 2010. Some of the projects are dealing with nanomaterials in food (www.NRP64.ch).

Safety provisions for use of nanomaterials in foods is covered by existing regulations and procedures. Pesticides are subject to an approval procedure which specifically asks for nanospecific information. The use of additives and ingredients in food is in part regulated with lists which provide information about whether a substance may or may not be used and whether quantitative restrictions apply. So far, the Federal Office of Public Health has not received any requests for approval of food additives containing nanomaterials. Possible future requests would be handled analogously to those for a new, as-yet unlisted additive. The same would apply to requests for packaging materials containing nanomaterials which come into contact with foodstuffs.

According to the Chemicals Ordinance, manufacturers of new and existing chemical substances and preparations are obligated to review the safety for consumers and the environment within the scope of their compulsory self-regulation. Nanomaterials corresponding to the new substance definition are subject to registration, and the data set necessary for the notification of new substances and for the declaration of substances and preparations classified as dangerous has been amended with data on the identity of nanomaterials recently.

Since April 2012 the central federal information platform for nanotechnology InfoNano is online. InfoNano provides information in German, French, Italian and English about the opportunities and risks associated with nanotechnology and synthetic nanomaterials. It is aimed at promoting the dialogue among administrative, economic, research and societal stakeholders (www.infonano.ch).

3.14 United States of America

Risk management

In addressing issues raised by nanomaterials, United States agencies adhere to the principles for regulation and oversight of emerging technologies, as summarized by Holdren, Sunstein & Siddiqui (2011).

The United States government founded the National Nanotechnology Initiative 10 years ago to leverage the research programmes on nanotechnology (Tinkle & Carim, 2011). In October 2011, the National Nanotechnology Initiative released a national strategy for ensuring the responsible development of nanotechnology and to support regulatory decision-making (NSET/NEHI, 2011). The 2011 strategy, which revises and replaces the 2008 strategy, concerns environmental, health and safety issues. The report identified that more research is required to develop tools for the determination of the physicochemical properties of engineered nanomaterials and for the detection and monitoring of engineered nanomaterials in realistic exposure media. In terms of human exposure assessment, the report recognized that more research is needed to understand the processes and factors that determine exposures to nanomaterials. In relation to human health, the most important research need is to identify or develop appropriate, reliable and reproducible in vitro and in vivo assays and models to predict in vivo human responses to engineered nanomaterials. Relating to risk assessment and risk management methods, more safety evaluation of nanomaterials is needed, with incorporated hazard identification, exposure science and risk modelling (NSET/NEHI, 2011).

Risk management: FDA

In June 2011, the United States Food and Drug Administration (FDA) issued for public comment a draft guidance document on considering whether an FDA-regulated product contains nanomaterials or otherwise involves the use of nanotechnology. According to the FDA, the guidance document does not establish any regulatory definitions. Rather, it is intended to help industry and others identify when they should consider potential implications for regulatory status, safety, effectiveness or public health impact that may arise with the application of nanotechnology in FDA-regulated products. The draft guidance document is intended to be broadly applicable to all FDA-regulated products, including food substances. According to this draft guidance document (FDA, 2011a):

"…when considering whether an FDA-regulated product contains nanomaterials or otherwise involves the application of nanotechnology, FDA will ask:

1. Whether an engineered material or end product has at least one dimension in the nanoscale range (approximately 1 nm to 100 nm); or
2. Whether an engineered material or end product exhibits properties or phenomena, including physical or chemical properties or biological effects, that are attributable to its dimension(s), even if these dimensions fall outside the nanoscale range, up to one micrometer."

The FDA's consumer update from June 2011 stated that the agency plans to develop additional guidance for specific products, as needed, in the future. The FDA is working with the White House, the National Nanotechnology Initiative, other United States government agencies and international regulators to focus on generating data and coordinating policy approaches to ensure the safety and effectiveness of products using nanomaterials (FDA, 2011b).

The draft guidance on substances to be used in dietary supplements, published in July 2011, proposes to include issues related to nanotechnology, if such use of nanotechnology results in new or altered properties of the ingredient (FDA, 2011c).

The FDA is in the process of preparing another guidance document that addresses the impact that manufacturing changes, including a change in particle size, would have on the regulatory status of authorized materials, which will address nanomaterials (A. McCarthy, FDA, personal communication, 2011). A corresponding draft guidance was published for public comments (FDA, 2012).

Risk assessment: FDA

The FDA does not maintain a list of nanomaterials that it has assessed (A. McCarthy, FDA, personal communication, 2011).

Risk management and assessment: EPA

The nanomaterial research strategy from 2009 defines the United States Environmental Protection Agency's (EPA) nanotechnology research programme to conduct focused research on nanomaterial safety (EPA, 2009). The EPA has identified five nanomaterial types for investigation that are widely used in products or have been recognized for their potential uses (EPA, 2011c). The materials being studied are:

1. ***Carbon tubes and fullerenes:*** Carbon materials have a wide range of uses, ranging from composites for use in vehicles and sports equipment to integrated circuits for electronic components.
2. ***Cerium oxide:*** Nano cerium is being investigated for uses ranging from drug delivery to automobile catalytic converters. One use currently on the market in some countries is as a diesel fuel additive to reduce exhaust particulates and increase fuel mileage.
3. ***Titanium dioxide:*** Nano titanium dioxide is currently used in many products. Depending on the type of particle, it may be found in sunscreens, cosmetics, and paints and coatings. It is also being investigated for use in removing contaminants from drinking-water.
4. ***Silver:*** Silver has long been known for its antimicrobial properties. Nanosilver is being incorporated into textiles and other materials to eliminate bacteria and odour from clothing, food packaging and other items where antimicrobial properties are desirable. The EPA has approved the use of a nanosilver-based antimicrobial product that is incorporated into textile as long as the company performs some required studies during the period of conditional registration (EPA, 2011a). Before this assessment, the EPA registered all silver particles applying risk assessment of ionic silver, without consideration of the particle size (Costanza, 2012).

5. ***Iron:*** While nanoscale iron is being investigated for many uses, including "smart fluids" for uses such as optics polishing and as better-absorbed iron nutrient supplements, one of its more prominent current uses is to remove contamination from groundwater. This use, supported by EPA research, is being piloted at a number of sites across the country.

EPA research will determine whether these materials present a potential environmental hazard or exposure over their life cycles and how these materials, when used in products, may be modified or managed to avoid or mitigate potential human health or ecological impacts.

Researchers in the EPA's Nanotechnology Research Program are studying nanomaterials to understand the potential unintended consequences from accidental or intentional exposure of humans. The research programme has the following approach for assessing the potential toxicity of nanomaterials:

- Identify and characterize the physical and chemical properties of manufactured nanomaterials.
- Identify alternative testing methods and approaches to predict toxicity in humans, which includes identification of biomarkers of nanomaterial exposure and/or toxicity.
- Assess the toxicity of nanomaterials in animals. These studies will include research to identify host susceptibility and sensitivity factors that may influence toxicity.

For a comprehensive environmental assessment, the EPA conducted two case-studies on titanium dioxide. One examined nano titanium dioxide use for water treatment, and the other looked at its use as an ingredient in sunscreens (EPA, 2010). The case-studies incorporated a comprehensive environmental assessment framework, which combines a product life cycle perspective with the risk assessment paradigm. This document will be used as part of a process to identify and prioritize research needs in developing data to inform nanomaterial risk assessment (OECD, 2011b).

In the *Federal Register* on 17 June 2011, the EPA's Office of Pesticide Programs proposed several approaches to obtain information on what nanoscale materials are present in pesticide products and requested comments from stakeholders (EPA, 2011b).

In the *Federal Register* on 26 October 2011, the EPA requested information on the discharge of nanosilver (an from industrial manufacturing) (EPA, 2011d). The EPA is interested in collecting as much information as possible on the fate, transport and effects of nanosilver on the aquatic environment and human health.

The National Research Council performed an independent study for the EPA to develop a research strategy to address the environmental, health and safety aspects of engineered nanomaterials. The comprehensive report summarized the current state of the science and identified research that needs to be undertaken and the resources needed (NRC, 2012). Relating to food, the report concluded that little is known about ingestion exposures and the transport and distribution of engineered nanomaterials in the human body. It was identified that research is needed to understand the biomolecular modifications of engineered nanomaterials in the human body.

4. Relevant activities by international governmental and nongovernmental organizations since 2009

4.1 Institute of Food Technologists

In the last few years, the Institute of Food Technologists (IFT) has supported research and published several articles on nanotechnology relating to an ongoing project on safety assessment:

- "Proposed minimum characterization parameters for studies on food and food-related nanomaterials" (Card & Magnuson, 2009);
- "A method to assess the quality of studies that examine the toxicity of engineered nanomaterials" (Card & Magnuson, 2010);
- "An appraisal of the published literature on the safety and toxicity of food-related nanomaterials" (Card *et al.*, 2011);
- "A brief review of the occurrence, use and safety of food-related nanomaterials" (Magnuson, Jonaitis & Card, 2011).

IFT offers an on-demand online course entitled "Introduction to Nanoscience" that provides an introduction to the subject and addresses fabricating and characterizing nanomaterials and nanoscience application challenges (http://www2.ift.org/PersonifyEbusiness/OnlineLearning/ LearnOnline/FoodScienceCourses/Description/tabid/364/Default.aspx?ProductId=1198). An on-demand webcast entitled "Nanoscience as an Emerging Food Industry Driver" addresses defining and describing nanoscale science and technology, applications and challenges facing the food industry (http://www2.ift.org/PersonifyEbusiness/OnlineLearning/LearnOnline/OnDemandWebcasts/Description/tabid/377/Default.aspx?ProductId=862).

Furthermore, IFT has held meetings and conferences that highlighted recent advances in safety and toxicological assessment of nanomaterials relevant to food application. Since 2006, IFT has organized an International Food Nanoscience Conference in conjunction with the IFT Annual Meeting & Food Expo. The fifth IFT International Food Nanoscience Conference was held in Chicago, Illinois, in July 2010. It focused on advances in safety and toxicological assessment of nanomaterials for food and food-related applications, the current regulatory guidelines in the United States and Europe and their legal implications for industry and other stakeholders, and investments

in nanotechnology research and development initiatives worldwide (Bugusu, 2010). IFT is in the process of initiating planning for the next International Food Nanoscience Conference, which will be convened in summer of 2013 in Chicago (R. Newsome, IFT, personal communication, 2012).

At the IFT Annual Meeting & Food Expo that took place in June 2011, several scientific sessions were held, and the following nanotechnology-related presentations were given:

- "Development of nanoengineered surfaces and evaluation of the effect of nanoscale topography on the attachment of pathogenic and biofilm-forming bacteria" (Moraru, 2011);
- "Carbohydrate nanoparticle-mediated colloidal assemblies to deliver antimicrobial peptide" (Yao, 2011);
- "Development and application of food-grade antimicrobial nanoparticles" (McClements, 2011);
- "Self-sanitizing food processing surfaces" (Goddard, 2011);
- "Overview of the science and technology in food and food products at the nanoscale level" (Yada, 2011);
- "Issues and challenges for food product applications of nanomaterials" (Magnuson, 2011);
- "Novel nanoscale structures inspired by biological systems" (Batt, 2011);
- "Diverse applications of DNA-based nanobiomaterials" (Luo, 2011);
- "Processing and characterization of nanostructured food materials" (Padua, 2011).

In addition to the above-mentioned scientific literature and conferences, IFT is supporting the development of a framework for implementing standard characterization of and reporting for nanomaterials. Referred to as the NanoCharacter project, this activity, which is in an initial stage, is being led by the International Life Sciences Institute (ILSI) Research Foundation (R. Newsome, IFT, personal communication, 2011; see also next section).

4.2 International Life Sciences Institute

The NanoRelease project from the ILSI Research Foundation's Center for Risk Science Innovation and Application aims to promote the safe development of nanomaterials by supporting the development of methods to understand the release of nanomaterials used in products. As part of the NanoRelease project, data, methods, guidance, standards and links are collected. The NanoRelease Steering Committee is composed of risk management experts from government, industry, nongovernmental organizations and international organizations (ILSI, 2011).

In a white paper providing background on the state of the science for nanomaterial release measurement, published on the ILSI web site, it is stated that "At the time of writing, there were over 3,500 studies that investigated nanoparticle release. However, nearly all of these research efforts focused on release in a targeted drug therapy context and less than 20 focused on release from consumer products" (Froggett, 2011).

The NanoRelease project is currently evaluating multiwalled carbon nanotube release from consumer products. The project is planning to undertake similar evaluation of engineered nanomaterial release from food matrices in the gastrointestinal tract (R. Canady, ILSI, personal communication, 2011). In the NanoCharacter project, the Center for Risk Science Innovation and Application has collected leading experts in nanotechnology environmental, health and safety research to develop a framework and road map for the staged implementation of consistent nanomaterial characterization and reporting practices. Over the course of the coming years, the road map will lay out the steps that need to be taken for funding, standardization, instrumentation, regulatory specifications and journal review so that studies use consistent methods for measuring physical properties to facilitate inter-study comparisons. More recently, a NanoRelease Food Additive project was launched that is evaluating and developing methods to characterize nanomaterials released from food in the gut (R. Canady, ILSI, personal communication, 2011).

NanoCharacter is another project aimed at developing a framework and road map for implementing widespread adoption of principles of reporting characteristics of nanomaterials in studies of commercial nanoproducts. The project builds on Organisation for Economic Co-operation and Development (OECD), International Organization for Standardization (ISO), Minimum Information on Nanoparticle Characterization (MINChar) and other efforts to establish "the list" of what to measure and will lay out how to get from concept to reality of consistent reporting. The project was initiated in response to a study of nanoparticle research in foods and will target food additives as one of the areas where consistent reporting is needed. A workshop is planned for August 2012 to draft a first framework document (R. Canady, ILSI, personal communication, 2011).

ILSI Europe initiated the Novel Foods and Nanotechnology Task Force (ILSI Europe, 2011), which started its work focusing on new technologies for the safety/nutritional assessment of novel foods and food ingredients. The aim of the activity will be to:

- review the applicability of new technologies for generating data and for integrating new types of data for safety (risk-based) and nutritional assessment;
- understand the role that other new and emerging technologies (e.g. tissue engineering, micro-ribonucleic acid, stem cells) may play in assessments in the future.

The brief on this activity is currently under development (A. Chiodini, ILSI, personal communication, 2011). This expert group previously discussed guidance for the safety assessment of engineered nanomaterials in food and developed a manuscript that was reviewed at a workshop that took place on 13–15 April 2011 in Cascais, Portugal, by participants from academia and industry, national authorities and representatives from the European Commission and EFSA. The expert group considered the outcome of the workshop discussions for the finalization of the article, which was on "Approaches to the safety assessment of engineered nanomaterials (ENM) in food" (Cockburn *et al.*, 2012).

The task force's proposal for the safety assessment of engineered nanomaterials involves five steps. In step 1, all available and relevant data for the material are collected.

In step 2, the physical and chemical characterization of the nanomaterial is conducted. In step 3, with the help of a decision-tree, this available information on physicochemical properties (especially solubility in water), data on bioavailability and comparison with existing "non-nano" versions of the material in question are used to decide what safety assessment approach is adequate. From this decision-tree, three scenarios follow: (i) if the nanomaterial's dissolution (rate, location) is comparable with that of the conventional material, it should be covered by the previous risk assessment for that material; (ii) if the nanomaterial's dissolution (rate, location) differs from the behaviour of the conventional material, a re-evaluation of the existing risk assessment with particular emphasis on absorption is advisable; and (iii) if the engineered nanomaterial is insoluble or partly insoluble, a tiered assessment addressing potential specific hazards is foreseen. In step 4, for materials for which at step 3 the existing risk assessment has been found not to cover the novel nanomaterial, a two-tiered testing scheme is used. At tier 1, the potential hazards are investigated in in vitro and short-term (<28 days) in vivo studies. At tier 2, if needed, the engineered nanomaterial is evaluated in more detail involving, as a minimum, a 90-day study in rodents and other focused and mechanistic studies. In the final step 5, an overall safety assessment of the engineered nanomaterial as consumed in food is described that takes into account the interaction with the food matrix (all components), the impact on solubility/bioavailability at local and systemic levels and the exposure to the engineered nanomaterial from food (A. Chiodini, ILSI, personal communication, 2011; FAO/WHO, 2012).

4.3 International Organization for Standardization (ISO)

ISO established in 2005 the *Technical Committee 229 Nanotechnologies* with the scope of standardization in the field of nanotechnologies that includes either or both of the following:

> "Understanding and control of matter and processes at the nanoscale, typically, but not exclusively, below 100 nanometres in one or more dimensions where the onset of size-dependent phenomena usually enables novel applications,
>
> Utilizing the properties of nanoscale materials that differ from the properties of individual atoms, molecules, and bulk matter, to create improved materials, devices, and systems that exploit these new properties."

Specific tasks include developing standards for: terminology and nomenclature; metrology and instrumentation, including specifications for reference materials; test methodologies; modelling and simulations; and science-based health, safety, and environmental practices. Some of these standards are intended to be used for toxicological assessment and include also guidance on toxicological screening methods. Until end of 2012 thirty-three texts have been developed (isotc.iso.org/livelink/livelink/open/tc229).

National standardization organizations affiliated to ISO are as well active in areas of nanotechnology that may be relevant to food safety: as an example the British

Standards Institution (BSI) has published a new standard relating to the 'Detection and characterization of manufactured nano-objects in complex matrices' (PAS 139:2012, available from http://www.bsigroup.com).

4.4 Organisation for Economic Co-operation and Development (OECD)

OECD activities do not address food directly. OECD has two relevant working parties: (1) the Working Party on Nanotechnology and (2) the Working Party on Manufactured Nanomaterials. Both working parties do not have food as a main subject; nevertheless, OECD's work on the testing and assessment of nanomaterials can be used for food-related nanomaterial applications (M. Gonzalez, OECD, personal communication, 2011).

The Working Party on Nanotechnology has, since 2007, advised on emerging policy issues of science, technology and innovation related to the responsible development of nanotechnology (OECD, 2011c). It provides to members socioeconomic analysis of nanotechnology and the facilitation of international collaboration in research and development and science and technology policies. The project from the Working Party on Nanotechnology on "Regulatory Tools for Nanotechnology in Food and Medical Products" aims at creating and maintaining inventories that will include information regarding:

- current regulatory frameworks in place for regulating the use of nanotechnology in food and in medical products;
- current legislative regimes relevant to regulatory frameworks in place for regulating the use of nanotechnology in food and in medical products;
- government-supported research institutions related to nanotechnology in food and in medical products, including current and future research strategies, programmes and activities.

The inventories will assist the Working Party on Nanotechnology in identifying areas of shared interest and highlight opportunities for enhancing communication related to regulation and applications of nanotechnology in food and medical products. The report analysing the survey's results is currently in development (M. Gonzalez, OECD, personal communication, 2011).

OECD's Working Party on Manufactured Nanomaterials, established in 2006, concentrates on the human health and environmental safety implications of manufactured nanomaterials, mainly with regard to the chemicals sector. The Working Party on Manufactured Nanomaterials aims to ensure that the approach to hazard, exposure and risk assessment is of a high, science-based and internationally harmonized standard. Its programme seeks to promote international cooperation on the human health and environmental safety of manufactured nanomaterials and involves the safety testing and risk assessment of manufactured nanomaterials. It is a subsidiary group of, and receives its mandate from, the Chemicals Committee (OECD, 2011c).

The Working Party on Manufactured Nanomaterials is active in a number of different areas. The following summaries are a selection of topics that are related to food.

A more comprehensive description of all activities can be found at http://www.oecd.org/env/nanosafety.

OECD database on research into the safety of manufactured nanomaterials

The objective of this project is to develop a global resource for research projects that address environmental, human health and safety issues of manufactured nanomaterials. This database helps to collect research information, search details by categories (e.g. nanomaterials, test methods, themes), identify gaps and assist in future collaborative efforts. Besides experimental studies, the database includes projects relevant to comprehensive risk assessments of specific substances, risk mitigation measures, regulatory aspects, international standard setting and reports on public dialogues. The database was publicly launched in April 2009 and now includes data on more than 700 research projects (OECD, 2009).

Safety testing of a representative set of manufactured nanomaterials

The "Sponsorship Programme for the Testing of Manufactured Nanomaterials" involves OECD member countries, as well as some non-member economies and other stakeholders, with the goal to pool expertise and fund the safety testing of specific manufactured nanomaterials. In initiating this programme, the Working Party on Manufactured Nanomaterials agreed on a priority list of 13 manufactured nanomaterials for testing, based on materials that are in or close to the market, such as fullerenes, single-walled carbon nanotubes, silver nanoparticles, titanium dioxide, silicon dioxide and nanoclays (OECD, 2010c). In addition, a number of end-points were selected for their relevance in providing crucial information related to environmental and human health safety. Therefore, each selected manufactured nanomaterial will be tested for its physicochemical properties, environmental degradation and accumulation, environmental toxicology and mammalian toxicology. As part of the programme, a *Guidance manual for the testing of manufactured nanomaterials* has been developed (OECD, 2010b). The programme is in its first phase, and dossiers for each sponsored nanomaterial are under preparation (M. Gonzalez, OECD, personal communication, 2011).

The role of alternative test methods in nanotoxicology

This project addresses the use of alternative methods and integrated testing strategies for manufactured nanomaterials. It is focused on in vitro or other alternative methods for the reduction, refinement or replacement of animals in test approaches that could be further explored with respect to manufactured nanomaterials. An outcome of this project will be guidance on integrated testing strategies, which will focus on those manufactured nanomaterials currently sponsored through the Sponsorship Programme (M. Gonzalez, OECD, personal communication, 2011).

Manufactured nanomaterials and test guidelines

Through this project, OECD is carefully evaluating any concrete proposals for the development or revision of test guidelines and/or guidance documents, which need to

take into account existing information and results coming from the scientific community. A preliminary review of 115 OECD test guidelines has shown that most of them are suitable, but that, in some cases, modification will be needed for their applicability to manufactured nanomaterials. Because the information concerning the properties of nanomaterials and their effects is still being developed, for example, through the Sponsorship Programme described above, the process to move ahead is flexible and able to adapt new information. Therefore, some of the outcomes being made available are expected to be revised as new information becomes available. For example, the document *Preliminary guidance notes on sample preparation and dosimetry for the safety testing of manufactured nanomaterials* has been published; as new information becomes available, it will be incorporated into a revised version (OECD, 2010d).

Voluntary schemes and regulatory programmes

This project has examined various national voluntary reporting schemes and regulatory programmes to assess the safety of manufactured nanomaterials. To date, the main outputs of this project have been (1) the analysis of information-gathering initiatives on manufactured nanomaterials, which includes a table of comparison of information-gathering schemes; and (2) the report of the questionnaire on regulatory regimes for manufactured nanomaterials, including legislative features identified in legislation on regulatory oversight of nanomaterials/nanoproducts. Two documents were published in December 2011: *Regulated nanomaterials: 2006–2009* (OECD, 2011d) and *Information gathering schemes on nanomaterials: lessons learned and reported information* (OECD, 2011a).

Risk assessment

The overall objectives of this project are to evaluate risk assessment approaches for manufactured nanomaterials through information exchange and to identify opportunities to strengthen and enhance risk assessment capacity. Through this project, it is expected that the outcomes of the work of the other Working Party of Manufactured Nanomaterials projects will be integrated into an overall framework within which risks of manufactured nanomaterials are assessed, ensuring good practice across OECD countries and other interested parties.

The document *Important issues on risk assessment of manufactured nanomaterials* has been developed (OECD, 2012). This document aims to introduce the current practices and challenges with respect to the risk assessment of manufactured nanomaterials as well as strategies for assessing risk in circumstances where data are limited. Furthermore, this document makes clear the necessity of direct research on specific risk assessment issues in concert with current efforts to develop basic data sets.

Environmentally sustainable use of nanotechnology

The aim of this project is to investigate the potential benefits of applications based on the use of manufactured nanomaterials. The expected outcome is the development of tools and frameworks based on life cycle considerations for different nano-enabled applications

that either directly address an environmental problem or indirectly contribute to environmental objectives. As such, the project will address environmental benefits, sustainability and life cycle–related issues. Through this project, the Working Party on Manufactured Nanomaterials seeks to complement current working party work regarding the potential positive and negative impacts on the environment and health of certain nano-enabled applications at their different stages of development.

As part of this project, the document *National activities on life cycle assessment of nanomaterials* was compiled from delegations and was published in December 2011 (OECD, 2011b).

5. Scientific reviews addressing risk assessment of nanotechnologies in the food and agriculture sectors

Recent scientific reviews on risk assessment of nanotechnologies in the food and agriculture sectors confirm that information on this topic is limited (Tran & Chaudhry, 2010; Card *et al.*, 2011; Horie & Fujita, 2011; Magnuson, Jonaitis & Card, 2011; Morris, 2011; Rico *et al.*, 2011; Krug & Wick, 2011).

A review on the interaction of nanoparticles with edible plants found that understanding of plant toxicity is at the early stages. Few studies have been performed on the accumulation of engineered nanomaterials in crop plants such as rape, radish, lettuce, corn and cucumber (Rico *et al.*, 2011). Rico *et al.* (2011) noted that among the studied nanomaterials, the carbon-based nanomaterials fullerenes C_{70} and fullerols $C_{60}(OH)_{20}$ and most of the metal-based nanomaterials (titanium dioxide, cerium oxide, magnetite, zinc oxide, gold, silver, copper and iron) accumulated in the plants. These compounds stored in the plants can be transferred to consumers. Depending on the studied nanomaterial and plant, negative effects of the nanoparticles on the food crops were observed, such as reduced germination, reduced root growth and delayed flowering.

Card *et al.* (2011) evaluated published literature on the safety of oral exposure to food-related nanomaterials and found that there are currently insufficient reliable data to allow a clear safety assessment. Card *et al.* (2011) also considered that non-food-related engineered nanomaterials require evaluation of oral toxicity in light of possible contamination of the food supply. Morris (2011) concluded that the lack of information on the possible toxicity of nanomaterials makes it difficult to assess the safe or acceptable daily intake.

Chaudhry & Castle (2011) discussed potential benefits and risks of the food applications of nanotechnologies with an emphasis on the opportunities and challenges for developing countries. The authors identify tree categories of concern depending on digestibility, solubility, biopersistence, and likely systemic exposure.

According to Magnuson, Jonaitis & Card (2011), the literature on the safety of oral exposure to nanomaterials inadequately characterizes nanomaterials with insufficient physicochemical parameters, concluding that "Unless nanomaterials are adequately characterized, the results of the toxicology studies cannot be utilized to predict toxicity of other nanomaterials as changes in any of the characteristics may result in changes in biological activity".

Horie & Fujita (2011) reasoned that in vitro and in vivo tests with no characterization of the nanomaterial are meaningless; for example, metal oxide nanoparticles with the same chemical composition are likely to have different effects depending on the manufacturer. Therefore, at the present time, risk evaluation requires characterization of each substance and each product (Horie & Fujita, 2011).

There has been more interest in occupational health, such as nanoparticle toxicology in the lung, and less research has been published on nanomaterial toxicity in the gut. According to the review by Morris (2011), there is at present little information on the effect of antimicrobial nanomaterials such as nanosilver on normal microbial populations in the mouth and gut. Few studies have attempted to find a relationship between the presence of nano-sized particulate materials in food and the initiation and/or worsening of certain gut diseases, such as Crohn disease and irritable bowel syndrome. Studies have produced contradicting results; therefore, there is a requirement for considerable further research (Tran & Chaudhry, 2010).

The safety assessment of nanomaterials will depend on their adequately characterized chemical properties; critical parameters include biopersistence and digestibility. Based on the development of nano forms of trace minerals, the group led by D. Pereira at MRC Human Nutrition Research identified three different scenarios. Digestible, non-biopersistent nanomaterials such as nano forms of a salt will be digested (dissolve) prior to any cellular exposure; for cells and tissues, there will be no difference if compared with conventional forms. A second type of digestible, non-biopersistent nanomaterial, such as micellar nano formulations or ferritin, will only partially degrade in the gut; they may therefore be absorbed as nano structures but will be rapidly broken down in cells. A third type, non-digestible, biopersistent nanomaterials, may remain intact and will raise different issues, an important one being their adsorbed surface materials, which may be removed in the stomach and replaced in the gut by luminal molecules before cellular uptake (FAO/WHO, 2012).

The above-described scenarios would be part of the first principle identified by Krug & Wick (2011), the transport principle. The authors identified three principles that in their view describe specific aspects of the separate discipline of "nanotoxicology". The principle of transport requires an understanding of whether and in what form nanomaterials will enter into cells where they may elicit a toxic response. The second principle of the surface reflects the fact that for smaller particles with active molecules on their surface, the proportion of atoms or molecules that are exposed and may therefore react with biological structures increases exponentially with decreased diameter if the same amount is administered. The third principle of material states that changes in dimensions (i.e. going towards nano) will not have the same effects but will depend on the properties of the material and its composition, including impurities.

[1] Search for literature with [Topic=(toxicology) AND Title=(nano*, lung)] or [Topic=(toxicology) AND Title=(nano* intestin* or gut)] within the years 2009 and 2011 (http://wokinfo.com/, accessed 6 February 2011).

6. Conclusions and recommendations

The review of national and international scientific (i.e. risk assessment related) and regulatory (i.e. risk management) activities on applications of nanotechnology in food and agriculture that have been undertaken since 2009 demonstrates that progress has been made in all three major areas addressed by the joint FAO/WHO expert meeting in 2009.

6.1 Use of nanotechnology

The concepts of potential use of nanomaterials in food and the implied benefits for stakeholders including consumers have not changed significantly. The main areas, as summarized in Appendix 4 of the FAO/WHO (2010) report, remain valid. New products are being developed and claimed to enter the market, but the available data from published sources and databases do not allow verifying whether product ideas are just concepts, unsubstantiated claims, or are already resulting in exposure of consumers to food being produced with nanotechnology/nanomaterials at any significant rate.

Whether a product would be considered to be a nanomaterial or representing an application of nanotechnology also depends on available definitions applied by regulators. Several regulatory bodies have meanwhile introduced or proposed definitions of nanomaterials for regulatory purposes that reflect one of the two main issues of the discussion: whether the dimension of materials of nanometer scale or the change of the properties of materials due to smaller particle size is more relevant. One definition extends the possible range of materials of concern to dimensions that are 10 times higher than the nanoscale range of 1–100 nm that was defined by the 2009 expert meeting. There is a trend to apply in the definitions two criteria, an altered or new dimension at nanoscale and a concurrent change of properties due to the change of dimension. A true nanomaterial that requires the attention of regulators and a specific risk assessment would need to meet both criteria. This was not fully clarified by the definitions as discussed and proposed by the 2009 expert meeting, but the discussion did address this issue, which was reflected in the proposal of a tiered approach for classifying nanomaterials for risk analysis purposes. Such a tiered approach would apply several criteria, of which dimension and change of properties expected to result in a modified hazard identification

and characterization would be two important ones. Change of properties such as solubility (which may result in breaking apart into the nanomaterial's building blocks), or biodegradability/digestibility would differentiate nanomaterials and their associated hazards. Such a more nuanced approach would also allow addressing those natural nanoscale substances which are present in food for a long time.

6.2 Assessment of human health risks

The statement by the 2009 joint FAO/WHO expert meeting (FAO/WHO, 2010) that current risk assessment approaches were suitable to assess nanomaterials and nanotechnologies used in food is supported by those agencies/institutions that have investigated this issue in more detail. National and regional food safety agencies increased their focus during the past few years on investigating the implications of nanomaterials added to or used with food. Policies and guidance documents have been published that allow a better understanding of how risk assessment of nanomaterials will be performed in the future.

Significant progress was made by OECD, which provides the globally accepted testing guidelines for hazard identification and characterization of food chemicals, such as additives, pesticides and veterinary drugs, and other substances resulting in human exposure, such as cosmetic ingredients. OECD reviewed these guidelines and found them to be generally applicable for the testing of nanomaterials. Other research-oriented projects initiated by OECD will provide valuable insights into aspects of risk assessment specific to engineered nanomaterials.

The approach to be published by ILSI for nanomaterials to be used in food is interesting, as it tries to systematically review the information already available for conventional material and discusses what properties would allow extrapolation from conventional to novel nanomaterials. Further development and implementation of this concept may lead to reduced animal testing.

Whether the paradigm of testing materials in animals at a toxic dose, determining a no-effect level and applying an uncertainty factor to establish a safe intake for humans is applicable to all nanomaterials continues to be challenged. The tiered approaches that are discussed may allow in vivo testing for specific groups such as nano-salts of micronutrients to be waived.

With respect to the use of nanomaterials in agriculture and food production one should keep in mind that workers in food and feed processing and on farms, and animals receiving feed containing nanomaterials may be exposed to these materials not only via the oral route but also due to dust formation by inhalation into their lungs and topically on their skin.

The number of published risk assessments of products that are nanomaterials or contain particles that fall within applicable definitions is growing slowly. As agencies apply different strategies with respect to communication, it is difficult to develop a clear picture of the true number of substances assessed and the issues discussed that are specific for nanomaterials. Particle risk assessment is a new field; risk assessment has always been

done with defined chemicals, with no attention paid to particle size. There is not enough known about nanomaterial toxicity to be able to group the particles into low-toxicity or high-toxicity groups. Therefore, nanomaterial risk assessment currently needs to be done on a case-by-case basis, as size, shape, chemical composition, surface area and surface charge influence the toxicity of nanomaterials (Park *et al.*, 2010). With respect to the three different exposure routes, more risk assessment has been done for inhalation and dermal exposure and less for ingestion exposure, because there are more nanomaterial products on the market in textiles, cosmetics and sprays than in food and food contact materials.

The main areas of chemical risk assessment at the international level address food additives, pesticide residues, veterinary drug residues, some processing aids, such as enzymes, and occasionally micro-nutrients. Nanomaterials would be within the scope of such activities; for example, a nanoscale food additive could be addressed by the Joint FAO/WHO Expert Committee on Food Additives, and residues from a nanoscale pesticide could be addressed by the Joint FAO/WHO Meeting on Pesticide Residues. There are, however, some areas of food chemicals, such as materials in contact with foods (e.g. food packaging), that occasionally are addressed by FAO/WHO expert bodies, but for which no comprehensive and systematic programme is in place; for a "nano-plastic material" to be used in food packaging, there is no risk analysis framework at the international level currently in place.

6.3 Stakeholder confidence and dialogue

A key finding of the 2009 FAO/WHO expert meeting was that public confidence in engineered nanomaterials can be supported through institutional efforts to provide an overview of applications of nanotechnology in food and packaging that are transparent and allow public involvement (FAO/WHO, 2010). However, for this report, it was difficult to assess the extent to which engineered nanomaterials are already being used in the food and agriculture sectors. Inventories that register nanotechnology in consumer products are scarce; only one database is publicly available.

Besides inventories, mandatory labelling would lead to greater transparency for the consumer and enable consumer freedom of choice. However, mandatory labelling could also lead to the avoidance of the use of nanotechnologies in consumer products, including those that are beneficial (Gruère, 2011). So far, apart from the European Union, no country has set a regulatory framework for the mandatory labelling of nanomaterials in food (EU, 2011).

The mandatory labelling of materials that meet a definition that reflects only dimension (i.e. is not risk based) provides a new element in the discussion that might be of interest to the Codex Alimentarius Commission, as it could result in technical barriers to trade of foods to which nanomaterials have been added.

In a report on the European Commission's public online consultation among key stakeholders about nanomaterials, the majority of the 716 respondents regarded applications in agriculture and food with more scepticism than applications in other areas

(EC, 2010). The major concern was the possible toxicity of poorly understood nanomaterials.

In accordance with the recommendations of the Science and Technology Committee of the United Kingdom Parliament, it may be valuable to develop a database of information on nanomaterials in development, in collaboration with the food industry, to anticipate future safety assessment needs and to aid in the prioritization of research (United Kingdom Parliament, 2010).

6.4 Recommendations

Use of nanotechnology

Nanotechnology for use by the food and agri-sectors is developing rapidly although its use for products reaching the marketplace is difficult to verify and quantify. Unambiguous and credible information on progress should be documented and shared among international stakeholders Collaboration with other international organizations that maintain already databases would allow to pool and use resources efficiently.

Definitions of nanomaterials

Definitions of nanomaterials differ depending on different requirements with respect to risk management (e.g. need for pre-market authorization) and risk assessment (e.g. triggers for evaluations). FAO and WHO may seek further expert advice and agreement whether a nanomaterial used in food and agriculture requires a specific risk assessment beyond those commonly needed. A tiered approach or decision tree to support identification of the appropriate risk assessment approach to categories of nanomaterials could be of specific assistance to risk managers and risk assessors. Such expert advice will benefit from good case studies based on comprehensive data and would be less helpful if using assumptions and limited datasets with significant gaps.

Definitions of nanomaterials developed during the past years result in different risk management measures (such as need for pre-market authorization, labelling). The Codex Alimentarius Commission may wish to consider whether food safety aspects of nanomaterials, including definitions, should be addressed through the development of relevant recommendations, which could be used by regulators at the national level. It would be important to take into account that nanotechnology is considered to be a promising future technology by food and agri-sectors in developed and developing countries.

Assessment of human health risks

Several data gaps with respect to interaction between nanomaterials and food matrices, behaviours of nanomaterials in human body, methods to determine such interactions and behaviours, and the relevance of such data for risk assessment continue to exist. FAO and WHO may consider to facilitate and, if feasible, coordinate international collaboration and information exchange between scientists from academia, industry and authorities, to address such gaps. It needs to be recognized that novel technologies are

usually proprietary and inventors may not likely to provide any data during early phase of development.

For many products such as food additives or pesticides, risk assessment policies and procedures are implemented at international level by bodies, such as JECFA or JMPR, that lead the development of scientific standards applied to the safety evaluation of chemicals. JECFA has noted that neither the specifications nor the ADIs for food additives that have been evaluated in other forms are intended to apply to nanoparticulate materials (JECFA, 2007) and that the evaluations for such material need to be done on a case-by-case basis. Taking into consideration that the existing risk assessment paradigm as applied by JECFA and JMPR is appropriate to conduct risk assessment of nanomaterials, FAO and WHO may consider clarifying specific issues associated with the topic, such as the overall availability, quality and adequacy of data, and consider developing a tiered approach to address them.

In that respect, the review of testing guidelines for chemical risk assessments by OECD may have identified need for modifications and specific issues to be addressed on their applicability to nanomaterials. FAO and WHO may wish to ask their expert bodies (especially JECFA and JMPR) to consider the result of this review and to assess their impact on currently applied risk assessment approaches.

International collaboration

ISO is developing since 2005 a significant number of standards and guidelines that may have impact on the use of nanomaterials by the food and feed sectors. The Codex Alimentarius Commission, FAO and WHO, as appropriate, should seek a better understanding of this work and its relevance to their own activities in the area of food safety.

FAO and WHO are encouraged to strengthen the international collaboration in the area of nanomaterials and nanotechnology in food and agriculture. International efforts on risk assessment of nanomaterials and food may benefit from the experience gained at national and regional level. Should a sufficient number of case studies of risk assessments of commercial products become available with time, a review of approaches applied and results obtained could support development of risk assessment procedures acceptable to FAO and WHO members.

References

ABDI (Agência Brasileira de Desenvolvimento Industrial). 2010. Estudo Prospectivo Nanotecnologia. [In Brazilian] 394 p. Brasilia: Brazilian Agency for Industrial Development (http://www.abdi.com.br/Estudo/Estudo%20Prospectivo%20de%20Nanotecnologia.pdf, accessed 23 November 2011).

AFC. 2007. Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) on a request related to a 14th list of substances for food contact materials. 10 p. Parma, Italy: European Food Safety Authority (http://www.efsa.europa.eu/en/scdocs/doc/afc_op_ej452-454_14thlist_op_en,7.pdf, accessed 15 November 2011).

Allmaier, G., Maisser, A., Laschober, C., Massner, P. & Szymanski, W.W. 2011. Parallel differential mobility analysis for electrostatic characterization and manipulation of nanoparticles and viruses. *Trends in Analytical Chemistry*, 30(1): 123–132.

ANEC/BEUC. 2009. Nanotechnology—Small is beautiful but is it safe? Brussels: The European Consumer Voice in Standardisation (ANEC) and European Consumers' Organisation (BEUC) (http://www.anec.org/attachments/ANEC-PT-2009-Nano-002final.pdf, accessed 30 January 2012).

ANS. 2008.Scientific Opinion: Inability to assess the safety of a silver hydrosol added for nutritional purposes as a source of silver in food supplements and the bioavailability of silver from this source based on the supporting dossier. Scientific Statement of the Panel on Food Additives and Nutrient Sources added to Food (ANS). Parma, Italy: European Food Safety Authority (http://www.efsa.europa.eu/en/efsajournal/pub/884.htm, accessed 15 November 2011).

ANS. 2011. Scientific opinion on re-evaluation of calcium carbonate (E 170) as a food additive. Scientific Statement of the Panel on Food Additives and Nutrient Sources added to Food (ANS). Parma, Italy: European Food Safety Authority (http://www.efsa.europa.eu/en/efsajournal/pub/2318.htm,, accessed 15 November 2011).

Batt, C. 2011. Novel nanoscale structures inspired by biological systems. Presented at the IFT Annual Meeting & Food Expo, New Orleans, LA, USA, 11–15 June 2011. Chicago, USA: Institute of Food Technologists.

Bucatariu, C.A. 2011. Genetically modified organisms and nanotechnologies in food and feed: EU lessons learned [thesis]. Parma, Italy: European College of Parma Foundation.

Bugusu, B. 2010. Exploring food nanomaterials. *Food Technology*, 64(10): 44.

Card, J.W. & Magnuson, B.A. 2009. Proposed minimum characterization parameters for studies on food and food-related nanomaterials [Letter to the editor]. *Journal of Food Science*, 74(8): vi–vii.

Card, J.W. & Magnuson, B.A. 2010. A method to assess the quality of studies that examine the toxicity of engineered nanomaterials. *International Journal of Toxicology*, 29(4): 402–410.

Card, J.W., Jonaitis, T.S., Tafazoli, S. & Magnuson, B.A. 2011. An appraisal of the published literature on the safety and toxicity of food-related nanomaterials. *Critical Reviews in Toxicology*, 41(1): 20–49.

CEF. 2008. Scientific Opinion of the Panel on food contact materials, enzymes, flavourings and processing aids (CEF). 21st list of substances for food contact materials. Parma, Italy: European Food Safety Authority (http://www.efsa.europa.eu/en/efsajournal/pub/888.htm, accessed 15 November 2011).

Chaudhry, Q. & Castle, L. 2011. Food applications of nanotechnologies – An overview of opportunities and challenges for developing countries. *Trends in Food Science and Technology*, 22(11): 595–603.

Chaudhry, Q., Castle, L. & Watkins, R. (editors) 2010. *Nanotechnologies in Food*. London: Royal Society of Chemistry Publishers.

Cockburn, A., Klein, C., Radomski, M., Stamm, H., Wijnhoven, S., Wildemann, T., Bradford, R., Buck, N., Constable, A., Edwards, G., Haber, B., Hepburn, P., Holett, J. & Kampers, F. 2012. Approaches to the safety assessment of engineered nanomaterials (ENM) in food. *Food and Chemical Toxicology*, 50(6): 2224–2242.

Costanza, J. 2012. EPA's approach to nanosilver risk assessment and regulation. Presented at the BfR Conference on Nanosilver, Berlin, Germany, 8–9 February 2012. Berlin: Federal Institute for Risk Assessment (http://www.bfr.bund.de/cm/349/pesticide-registration-of-nanosilver.pdf, accessed on 31 December 2012).

Department of Science and Technology of the Republic of South Africa. 2011. The national nanotechnology strategy. Pretoria: Department of Science and Technology (http://www.dst.gov.za/images/pdfs/Nanotech.pdf,, accessed 23 November 2011).

Dudkiewicz, A., Tiede, K., Loeschner, K., Jensen, L.H.S., Jensen, E., Wierzbicki, R., Boxall, A.M.A. & Molhave, K. 2011. Characterization of nanomaterials in food by electron microscopy. *Trends in Analytical Chemistry*, 30(1): 28–43.

EC (European Commission). 2010. Report on the European Commission's public online consultation. Towards a strategic nanotechnology action plan (SNAP) 2010–2015. European Commission (http://ec.europa.eu/research/consultations/snap/report_en.pdf, accessed 6 December 2011).

EC. 2011. Commission Recommendation of 18 October 2011 on the definition of nanomaterial. *Official Journal of the European Union*, L 275: 38–40 (http://eur-

lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:275:0038:0040:EN:PDF,, accessed 25 October 2011).

EFSA (European Food safety Authority). 2009. Scientific opinion of the Scientific Committee on a request from the European Commission on the potential risks arising from nanoscience and nanotechnologies on food and feed safety. *EFSA Journal*, 958: 1–39 (http://www.efsa.europa.eu/de/scdocs/doc/958.pdf, accessed 25 October 2011).

EFSA Scientific Committee. 2011. Scientific Opinion on Guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain. *EFSA Journal,* 9(5): 2140 (http://www.efsa.europa.eu/en/efsajournal/doc/2140.pdf, accessed 25 October 2011).

EPA (United States Environmental Protection Agency). 2009. Nanomaterial research strategy. Washington, DC: EPA Office of Research and Development (EPA 620/K-09/011). (http://www.epa.gov/nanoscience/files/nanotech_research_strategy_final.pdf, accessed 7 November 2011).

EPA. 2010. Nanomaterial case studies: Nanoscale titanium dioxide in water treatment and in topical sunscreen (final). Washington, DC: EPA. (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=230972#Download, accessed 7 November 2011).

EPA. 2011a. Decision document. Conditional registration of HeiQ AGS-20 as a materials preservative in textiles. December 1, 2011. Washington, DC: EPA Office of Pesticide Programs, Antimicrobials Division (http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-1012-0064, accessed 12 December 2011).

EPA. 2011b. Pesticides; Policies concerning products containing nanoscale materials; opportunity for public comment. *Federal Register*, 76(117): 35383–35395. Washington, DC: EPA. (http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2010-0197-0001, accessed 12 January 2012).

EPA. 2011c. Types of nanomaterials under investigation by the EPA. Washington, DC: EPA. (http://www.epa.gov/nanoscience/quickfinder/nanomaterials.htm, accessed 7 November 2011).

EPA. 2011d. Notice of final 2010 Effluent Guidelines Program Plan. *Federal Register*, 76(207): 66286–66304. Washington, DC: EPA. (http://www.gpo.gov/fdsys/pkg/FR-2011-10-26/html/2011-27742.htm,, accessed 12 December 2011).

EU (European Union). 2011. Regulation (EU) No 1169/2011 of the European Parliament and of the Council of 25 October 2011 on the provision of food information to consumers, amending Regulations (EC) No 1924/2006 and (EC) No 1925/2006 of the European Parliament and of the Council, and repealing Commission Directive 87/250/EEC, Council Directive 90/496/EEC, Commission Directive 1999/10/EC, Directive 2000/13/EC of the European Parliament and of the Council, Commission Directives 2002/67/EC and 2008/5/EC and Commission Regulation (EC) No 608/2004. *Official Journal of the European Union*, L 304: 18–63 (http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:304:0018:0063:EN:PDF, accessed 6 December 2011).

FAO/WHO. 2010. FAO/WHO expert meeting on the application of nanotechnologies in the food and agriculture sectors. Potential food safety implications. Meeting report. Rome: FAO and WHO (http://whqlibdoc.who.int/publications/2010/9789241563932_eng.pdf, accessed 25 October 2011).

FAO/WHO. 2012. Joint FAO/WHO Seminar on Nanotechnologies in Food and Agriculture, 27 March 2012. Rome: FAO. (http://www.fao.org/fileadmin/user_upload/agns/news_events/Nano_Seminar_Agenda_FINAL.pdf)

FDA (United States Food and Drug Administration). 2011a. Considering whether an FDA-regulated product involves the application of nanotechnology. Draft guidance for industry. Silver Spring, MD, USA: FDA. (http://www.fda.gov/RegulatoryInformation/Guidances/ucm257698.htm#rationale, accessed 4 November 2011).

FDA. 2011b. FDA opens dialogue on 'Nano' regulation. Silver Spring, MD, USA: FDA. (http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm258462.htm, accessed 4 November 2011).

FDA. 2011c. Draft guidance for industry: Dietary supplements: New dietary ingredient notifications and related issues. Silver Spring, MD, USA: FDA, Centre for Food Safety and Applied Nutrition. (http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/DietarySupplements/ucm257563.htm, accessed 16 February 2012).

FDA. 2012. Guidance for industry. Assessing the effects of significant manufacturing process changes, including emerging technologies, on the safety and regulatory status of food ingredients and food contact substances, including food ingredients that are color additives. Draft guidance for industry. (http://www.fda.gov/downloads/Cosmetics/GuidanceComplianceRegulatoryInfo>rma>tion/GuidanceDocuments/UCM300927.pdf, accessed 1 February 2013).

Fletcher, N. & Bartholomaeus, A. 2011. Regulation of nanotechnologies in food in Australia and New Zealand. *International Food Risk Analysis Journal*, 1(2): 33–40.

FOEN (Federal Office for the Environment). 2010. Draft conceptual study: Environmentally compatible and safe disposal of waste generated by the manufacture as well as the industrial and commercial processing of synthetic nanomaterials. [in German or French only]. Federal Office of Public Health (FOPH), Switzerland. (http://www.bag.admin.ch/nanotechnologie/12171/12177/index.html?lang=en, accessed on 31 December 2012).

Food Safety Law of China. 2009. The Food Safety Law of the People's Republic of China. Procedural Law Research Institution at China University of Political Science and Law (http://www.procedurallaw.cn/english/law/200903/t20090320_196425.html, accessed 4 January 2012).

FOPH (Federal Office of Public Health). 2010. Information for Consumers on Nanomaterials: Results of the NANO-Dialogue Platform. (http://www.bag.admin.ch/nanotechnologie/12197/12501/index.html?lang=en, accessed on 31 December 2012).

Frewer, L., Norde, N., Fischer, A. & Kampers, F. (editors) 2011. *Nanotechnology in the Agri-Food Sector: Implications for the Future*. Wiley-VCH Verlag.

Froggett, S. 2011. *Review of release from solids embedded or coated with nanomaterials.* Washington, DC: International Life Sciences Institute Research Foundation. (http://www.ilsi.org/researchfoundation/documents/nanorelease%20background%20doc.pdf, accessed 26 October 2011).

FSANZ (Food Standards Australia New Zealand). 2011. *Nanotechnology and food.* Canberra and Wellington: Food Standards Australia New Zealand. (http://www.foodstandards.gov.au/consumerinformation/nanotechnologyandfoo4542.cfm, accessed 16 November 2011).

FSCJ (Food Safety Commission of Japan). 2010. A basic survey report on safety assessment information on the use of nanotechnology in the food sector. Conducted by the Toray Research Center as "A comprehensive study for ensuring food safety under the Cabinet Office Food Safety Commission (FY 2009)" for the Food Safety Commission of Japan. (http://www.fsc.go.jp/english/survey_programs/use_nanotechnology.pdf, accessed 16 January 2012).

Gilliland, D. 2012. Physicochemistry of nanoscaled elemental silver and colloidal silver forms. Presented at the BfR Conference on Nanosilver, Berlin, Germany, 8–9 February 2012. Berlin: Federal Institute for Risk Assessment.

Goddard, J. 2011. Self-sanitizing food processing surfaces. Presented at the IFT Annual Meeting & Food Expo, New Orleans, LA, USA, 11–14 June 2011. Chicago,USA: Institute of Food Technologists.

Government of Japan Council for Science and Technology Policy. 2006. Science and technology basic plan [provisional translation]. Tokyo: Government of Japan, Council for Science and Technology Policy (http://www8.cao.go.jp/cstp/english/basic/3rd-BasicPlan_06-10.pdf, accessed 8 November 2011).

Government of Japan Council for Science and Technology Policy. 2010. Japan's science and technology basic policy report. Tokyo: Government of Japan, Council for Science and Technology Policy. (http://www8.cao.go.jp/cstp/english/basic/4th-BasicPolicy.pdf, accessed 8 November 2011).

Government of the Republic of South Africa. 2008. Foodstuffs, Cosmetics and Disinfectants Amendment Act, 2007. *Government Gazette*, 512: No. 30822, 28 February 2008. (http://www.info.gov.za/view/DownloadFileAction?id=88587,, accessed 23 November 2011).

Gruère, G.P. 2011. Labeling nano-enabled consumer products. *Nano Today*, 6(2): 117–121.

Health Canada. 2011. Policy statement on Health Canada's working definition for nanomaterial. Ottawa: Health Canada. (http://www.hc-sc.gc.ca/sr-sr/pubs/nano/pol-eng.php, accessed 8 November 2011).

Höck, J., Epprecht, T., Furrer, E. and 18 others. 2011. Precautionary matrix for synthetic nanomaterials.Version 2.1. Berne: Federal Office of Public Health and Federal Office for the Environment (http://www.bag.admin.ch/nanotechnologie/12171/12174/index.html?lang=en, accessed 9 December 2011).

Holdren, J.P., Sunstein, C.R. & Siddiqui, I.A. 2011. Principles for regulation and oversight of emerging technologies. Memorandum for the heads of executive

departments and agencies from the Office of Science and Technology Policy, the United States Trade Representative and the Office of Information and Regulatory Affairs. (http://www.whitehouse.gov/sites/default/files/omb/inforeg/for-agencies/Principles-for-Regulation-and-Oversight-of-Emerging-Technologies-new.pdf, accessed 8 November 2011).

Horie, M. & Fujita, K. 2011. Toxicity of metal oxides nanoparticles. Chapter 4, *in: Advances in molecular toxicology.* Vol. 5. Elsevier B.V.

Huang, Q. (editor) 2012. *Nanotechnology in the Food, Beverage and Nutraceutical Industries*. Cambridge, UK: Woodhead Publishing Ltd.

IG DHS. 2011. Code of conduct: nanotechnologies. Berne: Interessengemeinschaft Detailhandel Schweiz. (http://www.igdhs.ch/m/mandanten/175/download/CoC_Nanotechnologien_final_16_01_09_e.pdf, accessed 9 December 2011).

ILSI (International Life Sciences Institute). 2011. Developing methods to measure release of nanomaterials from solid matrices. Washington, DC: International Life Sciences Institute Research Foundation. (http://www.ilsi.org/ResearchFoundation/Pages/NanoRelease1.aspx, accessed 26 October 2011).

ILSI Europe. 2011. Novel Foods and Nanotechnology Task Force. International Life Sciences Institute Europe. (http://www.ilsi.org/Europe/Pages/TF_NovelFoods.aspx, accessed 26 October 2011).

Japan Science and Technology Agency. 2010. Nanotechnology—Grand design in Japan: Key technology for solving global issues. Center for Research and Development Strategy, Japan Science and Technology Agency. (http://crds.jst.go.jp/singh/wp-content/uploads/10sp02e.pdf, accessed 8 October 2011).

Japanese Ministry of Agriculture, Forestry and Fisheries. 2007. Food Nanotechnology Project, MAFF. National Agriculture and Food Research Organization, Agriculture, Forestry and Fisheries Research Council (Japan). (http://www.naro.affrc.go.jp/org/nfri/yakudachi/foodnanotech/index_e.html, accessed 8 November 2011).

JECFA (Joint FAO/WHO Expert Committee on Food Additives). 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. (http://whqlibdoc.who.int/trs/WHO_TRS_940_eng.pdf)

JRC (European Commission, Joint Research Centre). 2011. Small material, big impact: European repository of reference nanomaterials will improve safety assessment [Press Release 14/02/11]. European Commission, Joint Research Centre. (http://ec.europa.eu/dgs/jrc/index.cfm?id=2300&obj_id=2950&dt_code=PRL&lang=en, accessed 15 February 2012).

Korean Ministry of Education, Science and Technology. 2011. The 3rd International Nanomaterials Ethics Workshop. Seoul: Korean Ministry of Education, Science and Technology. (http://english.mest.go.kr/web/42208/en/board/enview.do?scriptYn=&searchWord=nano&bbsId=265&lineCnt=10&encodeYn=N&currentPage=&mode=&y=26&x=26&password=&searchOption=content&boardSeq=20205&mode=view, accessed 23 November 2011).

Krug, H.F. & Wick, P. 2011. Nanotoxikologie – eine interdisziplinäre Herausforderung. *Angewandte Chemie*, 123: 1294–1314.

Linsinger, T.P.J., Roebben, G., Solans, C. & Ramsch, R. 2011. Reference materials for measuring the size of nanoparticles. *Trends in Analytical Chemistry*, 30(1): 18–27.

Luo, D. 2011. Diverse applications of DNA-based nanobiomaterials. Presented at the IFT Annual Meeting & Food Expo, New Orleans, LA, USA, 11–14 June 2011. Chicago, USA: Institute of Food Technologists.

Magnuson, B.A. 2011. Issues and challenges for food product applications of nanomaterials. Presented at the IFT Annual Meeting & Food Expo, New Orleans, LA, USA, 11–14 June 2011. Chicago,USA: Institute of Food Technologists.

Magnuson, B.A., Jonaitis, T.S. & Card, J.W. 2011. A brief review of the occurrence, use, and safety of food-related nanomaterials. *Journal of Food Science*, 76(6): R126–R133.

McClements, D.J. 2011. Development and application of food-grade antimicrobial nanoparticles. Presented at the IFT Annual Meeting & Food Expo, New Orleans, LA, USA, 11–14 June 2011. Chicago, USA: Institute of Food Technologists.

McClements, D.J. & Jiajia, R. 2011. Food-grade nano-emulsions: formulation, fabrication, properties, performance, biological fate, and potential toxicity. *Critical Reviews in Food Science and Nutrition*, 51(4): 285–330.

Moraru, C. 2011. Development of nano-engineered surfaces and evaluation of the effect of nanoscale topography on the attachment of pathogenic and biofilm-forming bacteria. Presented at the IFT Annual Meeting & Food Expo, New Orleans, LA, USA, 11–14 June 2011. Chicago, USA: Institute of Food Technologists.

Morris, V.J. 2011. Emerging roles of engineered nanomaterials in the food industry. *Trends in Biotechnology*, 29(10): 509–516.

NanoLyse. 2011. Nanoparticles in food: analytical methods for detection and characterisation. Project funded by the European Union's framework programme. (http://www.nanolyse.eu/default.aspx, accessed 26 October 2011).

NIA (Nanotechnology Industries Association). 2011. Brazilian Competitiveness Forum on Nanotechnology discusses nanotechnology regulation. Brussels: Nanotechnology Industries Association. (http://www.nanotechia.org/global-news/brazilian-competitiveness-forum-on-nanotechnology-discusses-nanotechnology-regulation, accessed 23 November 2011).

NRC (National Research Council). 2012. A research strategy for environmental, health, and safety aspects of engineered nanomaterials. Washington, DC: National Research Council. The National Academies Press. (http://www.nap.edu/catalog.php?record_id=13347&utm_medium=etmail&utm_source=National%20Academies%20Press&utm_campaign=NAP+mail+new+1.31.12&utm_content=&utm_term=, accessed 7 November 2011).

NSET/NEHI. 2011. NNI 2011 environmental, health, and safety (EHS) research strategy. United States National Nanotechnology Initiative, Nanotechnology Environmental and Health Implications Working Group of the Nanoscale Science,

Engineering, and Technology Subcommitt. (http://www.nano.gov/node/681, accessed 7 November 2011).

ObservatoryNANO. 2010. ObservatoryNANO factsheets 2009–2010. Project funded by the European Union's framework programme. (http://www.observatorynano.eu/project/document/3319/, accessed 2 December 2011).

ObservatoryNANO. 2011. ObservatoryNANO factsheets 2010–2011. Project funded by the European Union's framework programme. (http://www.observatorynano.eu/project/document/3484/, accessed 2 December 2011).

OECD (Organisation for Economic Co-operation and Development). 2009. OECD database on research into the safety of manufactured nanomaterials. Paris: OECD. (http://webnet.oecd.org/NanoMaterials/Pagelet/Front/Default.aspx, accessed 2 January 2012).

OECD. 2010a. Current developments/activities on the safety of manufactured nanomaterials. Paris: OECD. (http://www.oecd.org/officialdocuments/displaydocumentpdf?cote=env/jm/mono(2010)42&doclanguage=en, accessed 27 December 2011).

OECD. 2010b. Guidance manual for the testing of manufactured nanomaterials: OECD sponsorship programme; first revision. Paris: OECD. (http://www.oecd.org/officialdocuments/displaydocumentpdf?cote=env/jm/mono%282009%2920/rev&doclanguage=en, accessed 2 January 2012).

OECD. 2010c. List of manufactured nanomaterials and list of endpoints for phase one of the sponsorship programme for the testing of manufactured nanomaterials: revision. Paris: OECD. (http://www.oecd.org/officialdocuments/displaydocumentpdf/?cote=env/jm/mono(2010)46&doclanguage=en,, accessed 21 November 2011).

OECD. 2010d. Preliminary guidance notes on sample preparation and dosimetry for the safety testing of manufactured nanomaterials. Paris: OECD. (http://www.oecd.org/officialdocuments/displaydocumentpdf?cote=env/jm/mono%282010%2925&doclanguage=en, accessed 2 January 2012).

OECD. 2011a. Information gathering schemes on nanomaterials: lessons learned and reported information. Paris: OECD. http://www.oecd.org/officialdocuments/displaydocumentpdf?cote=env/jm/mono%282011%2953&doclanguage=en, accessed 2 January 2012).

OECD. 2011b. National activities on life cycle assessment of nanomaterials. Paris: OECD. (http://www.oecd.org/officialdocuments/displaydocumentpdf?cote=env/jm/mono%282011%2954&doclanguage=en, accessed 2 January 2012).

OECD. 2011c. OECD Working Party on Nanotechnology (WPN): vision statement. Paris: OECD. (http://www.oecd.org/document/35/0,3746,en_21571361_41212117_42378531_1_1_1_1,00.html, accessed 25 November 2011).

OECD. 2011d. Regulated nanomaterials: 2006–2009. Paris: OECD. (http://www.oecd.org/officialdocuments/displaydocumentpdf?cote=env/jm/mono%282011%2952&doclanguage=en, accessed 2 January 2012).

OECD. 2012. Important issues on risk assessment of manufactured nanomaterials. Paris: OECD. (http://www.oecd.org/officialdocuments/displaydocumentpdf?cote=env/jm/mono(2012)8&doclanguage=en, accessed 12 May 2012).

Padua, G. 2011. Processing and characterization of nanostructured food materials. IFT Annual Meeting & Food Expo, New Orleans, LA, USA, 11–14 June 2011. Chicago, USA: Institute of Food Technologists.

Park, E.J., Bae, E., Yi, J., Kim, Y., Choi, K., Lee, S.H., Yoon, J., Lee, B.C. & Park, K. 2010. Repeated-dose toxicity and inflammatory responses in mice by oral administration of silver nanoparticles. *Environmental Toxicology and Pharmacology*, 30(2): 162–168.

Peters, R., Hajslova, J., Weigel, S., ten Dam, G., Bouwmeester, H., Helsper, H., Allmaier, G., von der Kammer, F., Ramsch, R., Solans, C. & Tomaniova, M. 2011. Identification and characterization of organic nanoparticles in food. *Trends in Analytical Chemistry*, 30(1): 100–112.

Poto, M. 2011. Food and nano-food within the Chinese regulatory system: no need to have overregulation. *European Journal of Law and Technology*, 2(3) [Online; http://ejlt.org//article/view/81/181], accessed 2 January 2011.

Qian, G.X., Guo, X.C., Guo, J.J. & Wu, J.G. 2011. China's dairy crisis: impacts, causes and policy implications for a sustainable dairy industry. *International Journal of Sustainable Development & World Ecology*, 18(5): 434–441.

Rico, C.M., Majumdar, S., Duarte-Gardea, M., Peralta-Videa, J.R. & Gardea-Torresdey, J.L. 2011. Interaction of nanoparticles with edible plants and their possible implications in the food chain. *Journal of Agricultural and Food Chemistry*, 59(8): 3485–3498.

SCCS. 2011. Opinion on 1,3,5- triazine, 2,4,6-tris[1,1'-biphenyl]-4-yl-, 20 September 2011 (SCCS/1429/11). European Commission, Scientific Committee on Consumer Safety. (http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_070.pdf, accessed on 31 December 2012).

SCCS. 2012a. Opinion on zinc oxide (nano form) Colipa S76, 18 September 2012 (SCCS/1489/12). European Commission, Scientific Committee on Consumer Safety (http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_103.pdf, accessed on 31 December 2012).

SCCS. 2012b. Guidance on the Safety Assessment of Nanomaterials in Cosmetics. 26–27 June 2012. European Commission, Scientific Committee on Consumer Safety (http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_005.pdf)

SCENIHR. 2010. Scientific basis for the definition of the term "nanomaterial". European Commission, Directorate-General for Health & Consumers, Scientific Committee on Emerging and Newly Identified Health Risks. (http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_032.pdf, accessed 28 October 2011).

SECO (State Secretariat for Economic Affairs). 2012. Safety data sheet (SDS): Guidelines for synthetic nanomaterials, Version 2.0. SECO, Zurich, Switzerland.

(http://www.bag.admin.ch/nanotechnologie/12171/12176/index.html?lang=en, accessed on 31 December 2012).

Tinkle, S. & Carim, A. 2011. Responsible development of nanotechnology: maximizing results while minimizing risk. Washington, DC: Office of Science and Technology Policy. (http://www.whitehouse.gov/blog/2011/10/20/responsible-development-nanotechnology-maximizing-results-while-minimizing-risk, accessed 8 November 2012).

Tran, L. & Chaudhry, Q. 2010. Engineered nanoparticles and food: an assessment of exposure and hazard. Chapter 8, *in:* Q. Chaudhry, L. Castle and R. Watkins (editors). *Nanotechnologies in food.* The Royal Society of Chemistry, RSC Publishing.

Tutelyan, V.A. 2012. Russian Federation. The control over nanomaterials. Letter sent in reponse to the request for public review.

United Kingdom Parliament. 2010. *Nanotechnologies and food. Volume I: Report.* House of Lords, Science and Technology Committee, 1st report of session 2009–10. London: The Stationery Office Limited (http://www.publications.parliament.uk/pa/ld200910/ldselect/ldsctech/22/22i.pdf, accessed 6 December 2011).

von der Kammer, F., Legros, S., Larsen, E.H., Loeschner, K. & Hofmann, T. 2011. Separation and characterization of nanoparticles in complex food and environmental samples by field-flow fractionation. *Trends in Analytical Chemistry*, 30(3): 425–436.

Yada, R. 2011. Overview of the science and technology in food and food products at the nanoscale level. Presented at the IFT Annual Meeting & Food Expo, New Orleans, LA, USA, 11–14 June 2011. Chicago, USA: Institute of Food Technologists.

Yao, Y. 2011. Carbohydrate nanoparticle-mediated colloidal assemblies to deliver antimicrobial peptide. Presented at the IFT Annual Meeting & Food Expo, New Orleans, LA, USA, 11–14 June 2011. Chicago, USA: Institute of Food Technologists.

ee. (http://www.nano.gov/node/681, accessed 7 November 2011).

Following up on one of the recommendations of the 2009 FAO/WHO expert meeting, the present report reviews national and international activities on the risk analysis of nanomaterials in the food and agriculture sectors that have been carried out since the meeting.

It presents national and international risk assessment and risk management approaches that identify and implement strategies to address potential hazards associated with the use of nanotechnology-related products or techniques.

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