International Conference on Food and Agriculture Applications of Nanotechnologies

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**Report
of
Technical Round Table Sessions**

Organized by FAO in collaboration with

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i Acknowledgments

ADI	acceptable daily intake
ADME	absorption, distribution, metabolism, excretion
BM	benchmark
bw	body weight
CAPES	Brazilian Coordination for Development of Graduate Human Resources
CNT	carbon nanotube
EFSA	European Food Safety Authority
EHS	environmental and health safety
ENP	engineered nanoparticle
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FCM	food contact material
FoE	Friends of the Earth
FTAI	Fixed-Time Artificial Insemination
GRAS	generally regarded as safe
IOMC	Inter-Organization Program for the Sound Management of Chemicals
ISO	International Organization for Standardization
JECFA	Joint FAO/WHO Expert Committee on Food Additives
MRL	Maximum residue limit
MWCNT	multi-wall carbon nanotube
N&N	nanoscience and nanotechnology
NISEnet	Nanoscale Informal Science Education Network
NGO	non-governmental organization
NOEL	No-observed-effect level
NP	nanoparticle
OECD	Organisation for Economic Co-operation and Development
OIE	World Organisation for Animal Health
QD	quantum dots
QSAR	quantitative structure-activity relationship
RA	risk assessment
RFID	radio frequency identification display
RMF	risk management framework
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SEM	scanning electron microscope
SMEs	small and medium enterprises
SWCNT	single-wall carbon nanotube
TEM	transmission electron microscope
UNESCO	United Nations Educational, Scientific and Cultural Organization
USDA	United States Department of Agriculture
WHO	World Health Organization

iii Executive summary

A number of emerging nanotechnologies could potentially provide significant benefits in various sectors, including food, water and agriculture. New and emerging applications such as water purification systems, rapid pathogen and chemical contaminant detection systems, and nano-enabled renewable energy technologies applied along the food chain may be the new tools to address some of the challenges pertaining to sustainable agricultural development as well as food safety and food security that countries are facing today – in particular developing countries.

Research and development in nanoscience and nanotechnologies have been growing in the public and private sectors in both developed and developing countries. It is becoming clear that in order to achieve the expected goals promised by nanotechnologies, the world community must ensure that direct, forthright global governance of these technologies is addressed.

In the light of these developments, the Government of Brazil, in collaboration with FAO, organized an international conference as a forum on new and emerging applications of nanotechnologies in food, water and agriculture. The purpose of the conference was to facilitate among stakeholder groups an exchange of views and collaboration in promoting progress in areas that are of particular interest to developing countries.

The conference aimed to:
– identify those emerging nanotechnology applications which are considered as having the greatest potential in providing broad equitable social benefits;
– promote collaboration and partnerships among countries on issues of common interest; and
– promote a harmonized approach toward the assessment and management of potential human health and environmental risks that may be associated with the application of nanotechnologies in the areas of food and agriculture.

The conference brought together approximately 200 participants, from over than 20 countries, with different backgrounds and perspectives on nanotechnologies in food, water and agriculture. FAO, in collaboration with EFSA, IUFoST and OECD, organized three technical round-table sessions with 22 experts from academic institutions, the private sector, government organizations, international organizations and non-governmental organizations (NGOs) to discuss the following themes:
1. Food "nano"-applications: ensuring broad social benefits
2. Nanotechnologies in agriculture: new tools for sustainable development
3. Nanotechnologies: the regulatory framework

Round Table 1 focused on three categories of applications potentially capable of potentially providing significant benefits to the food sector and consumers:
• Treatment of drinking water and of water for use in food processing
• Packaging materials for food and other food contact materials
• Nano-(bio) sensors and tracking systems for food products

Concerning the future of water nano-applications in developing countries, participants recognized the need to conduct pilot feasibility studies and to improve the understanding of how these technologies could best be adapted to meet developing countries' needs within specific social, technological and economic contexts. Furthermore, it is crucial to exercise all necessary diligence to ensure that nanotechnologies improve material and social conditions without exceeding the ecological capital that supports them, and also to proactively assess and mitigate potential human and environmental risks in the early stages of the development of these technologies.

Packaging materials incorporating nanoparticles (NPs) and nanostructures were recognized as offering a series of advantages over existing materials, including lighter weight, better protection and preservation of food, and hence reduced food waste and transport costs. However, many questions must still be answered as there is a lack of information concerning NP migration from packaging materials to foods as well as uncertainties related to hazard identification and characterization of NPs and exposure levels. Moreover, potential environmental impact resulting from the disposal of NP-containing food packaging as well as recycling and re-use of these materials are issues that must still be addressed.

Nano-sensors, developed through the integration of nanotechnologies with molecular biology and information technology, could provide food-chain operators and food safety authorities with the tools to rapidly detect pathogens and potential contaminants, including chemical/biological agents. It was noted that the costs of such sensors would drop dramatically with substantial demand: the round-table experts stated that there is currrently not a strong demand from the agri-food sector. The technology is already sufficiently advanced to enable specific sensors to be developed within a relatively short time (one year) once reliable signals of demand from the food sector are received. These sensors can offer a range of advantages to both developing and developed countries, such as rapid response time, simplicity of use, and robustness and suitability for field use.

Round Table 2, which dealt with nanotechnology applications in agriculture, identified five main areas where more research and work should contribute to overcoming challenges to sustainable agricultural development, namely plant production; animal productcion; value-added products; the environment; and education, communication and training.

Nanotechnologies in plant production may contribute to improved control in using agrochemical inputs. Significant progress has already been achieved in the area of nanoencapsulation and nanostructured carriers for controlled release of pesticides and fertilizers.

In animal production there are a number of significant challenges for nanotechnology, including production efficiency, animal health, feed nutrition efficiency, diseases (including zoonoses), product quality and value, by-products and waste, and environmental footprints, for which nanotechnologies may offer effective solutions. In particular, nanoscale delivery systems applied to existing technologies for artificial insemination can significantly improve animal fertility. Another critical element of sustainable animal production is the improvement of feeding efficiency. Here again nanotechnologies may offer significant

improvements by facilitating better utilization of proteins and micronutrients and improving overall health of animals so that an optimal physiological state can be maintained.

Discussion also focused on the possibilities offered by nanotechnologies for renewable energy such as nanotechnology-based photovoltaic energy to be used in post-harvest operations (drying, storage, preservation of agricultural products). However, many obstacles must be overcome in order to improve efficiency, reduce costs, and make these applications feasible for developing countries.

Round Table 3 addressed the challenges in ensuring the effective regulation of food products developed with nanotechnologies, and in promoting a harmonized approach among countries for regulating such products, namely:
1. Risk/safety assessment of nanoparticles and data requirements for approval processes
2. Terminology and definitions related to nanotechnologies and implications for regulation and labelling
3. Challenges to enforcement

While the existing risk assessment principles and methodologies are considered appropriate for engineered nanomaterials, clearer guidance on safety testing methods and more exposure assessment data due to our limited knowledge of the human health effects of NPs are needed. A more coordinated approach at the international level needs to be promoted among institutions, including participating organizations of the Inter-Organization Programme for the Sound Management of Chemicals (IOMC[1]), such as FAO, OECD and the World Health Organization (WHO) , as well as independent agencies such as EFSA that are currently working on a tiered approach for risk assessment of categories of nanomaterials and on the development of a decision-tree to guide the risk assessment process.

On the safety requirements for market-entry, clearer articulation of data required for approval processes, as well as an internationally accessible database in which to collate all relevant data and official information on national and regional requirements are necessary.

On the terminology and definitions of nanotechnologies, there was some agreement that even without agreed definitions for nano-particles or nanostructures, regulatory frameworks can still capture and therefore regulate nanotechnology applications. Other panellists instead reiterated the need for agreed definitions in order to effectively regulate this area. Some experts also requested that international organizations that are already working on the development of nano-definitions (e.g. International Organization for Standardization Technical Committee (ISO/TC) 229 Nanotecnologies) work together on a glossary of terms for nanotechnologies.

One of the most urgent challenges identified in relation to enforcing a regulatory framework is the lack of routine detection methods of NPs in foods. The group suggested that, while the

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[1] IOMC serves as a mechanism for initiating, facilitating and coordinating international action for sound management of chemicals. FAO, OECD and WHO are Participating Organizations. More information is available at: http://www.who.int/iomc/en/

industries and producers need to strongly commit to developing suitable nanotechnology detection methods, in the absence of such methods it will be necessary to use existing traceability systems.

This round-table discussion also recognized that the existing regulatory uncertainties could result in additional challenges for small- and medium-sized enterprises (SMEs), which might be not be able to invest if they are required to comply with the regulatory approval processes. At the same time, it was acknowledged that efficient regulatory systems capable of assessing, tracking and monitoring nanotechnology applications in food and agriculture can be costly, and many countries lack the infrastructure, funds and capacity for setting up and implementing such systems.

The participants of all three round tables considered that advances in nanotechnologies could offer potential for developing countries to innovate and add value to their current commodities and food production systems, but potentially pose significant challenges. While nanotechnologies may improve efficiency in some areas, they may not necessarily solve the existing problems of global food production and distribution. Therefore, it is necessary to consider the social and ethical implications of new agriculture technologies. In this regard, to facilitate access by developing countries to new and promising applications, the experts suggested setting up an international forum to agree on a shared vision and provide guidance on management of global issues, as a platform to discuss nano-relevant issues involving all countries, developing and developed. The experts also concluded that all stakeholders should seek technological solutions that build on local knowledge and capacities, ensuring that nanotechnologies complement existing technologies.

The outcomes of the conference will be used by FAO and other international organizations as a base for future action, including developing partnerships and collaboration among countries on those nano-applications identified as beneficial; contributing to an international exchange platform for sharing information and discussing issues of global relevance (e.g. public domain of information, knowledge and needs to preserve a large field of public information); and contributing to an international coordinated effort to review and define the tiered approach for assessing the risks of nanotechnologies.

1 Introduction

1.1 Background

A number of emerging nanotechnologies seem to be capable of potentially providing significant benefits in various sectors including food, water and agriculture. New and emerging applications such as water purification systems, rapid pathogen and chemical contaminant detection systems, and nano-enabled renewable energy technologies applied along the food chain are expected to provide developed and developing countries with new tools to address some of the challenges to sustainable agricultural development as well as food safety and food security.

Research and development in nano-science/nanotechnologies have been growing worldwide in the public and private sectors within developed as well as emerging countries. Many countries have in fact recognized the potential of nanotechnologies in the food and agriculture sectors, and are investing significantly in their applications to food production. However, the potential implications of nanotechnologies on human and environmental health have recently raised growing concerns in the international community. As there is limited knowledge of the human health effects of these applications, many countries have stressed the need for early consideration of the food safety implications of the technology. In response to such requests, FAO and WHO held an Expert Meeting on the "Application of nanotechnologies in the food and agriculture sectors: potential food safety implications" in June 2009.
http://www.fao.org/ag/agn/agns/files/FAO_WHO_Nano_Expert_Meeting_Report_Final.pdf

Human health effects of nanotechnologies are not, however, the only concern related to their applications in food and agriculture. Environmental health, social and ethical implications, challenges for developing countries and the need for adequate and immediate attention to global governance are some of the crucial issues that need to be addressed at the international level, if the expected gains from nanotechnologies in the areas of food, agriculture and human health are to be realized.

With this background, the Government of Brazil, in collaboration with FAO, organized an international conference as a forum for debate and discussion on new and emerging applications of nanotechnologies in food, water and agriculture. The purpose of the conference was to facilitate communication and collaboration among stakeholder groups in promoting progress in areas that are of particular interest to developing countries.

In the preparation and implementation of the round-table sessions, FAO was supported by the EFSA, IUFoST and OECD. These three institutions are involved in the debate surrounding nanotechnologies, and their different programmes and activities in the area are briefly described below.

EFSA produces scientific opinions and advice to support the European Commission, European Parliament and European Union Member States in taking risk management decisions in the area of food safety (http://www.efsa.europa.eu/). Since 2006, EFSA has been following developments in nanotechnology within its mandate, including reviewing the

current state of knowledge and latest developments in nanotechnology with regard to food and feed. In 2009 EFSA published a scientific opinion on nanoscience and nanotechnologies in relation to food and feed safety (http://www.efsa.europa.eu/en/scdocs/scdoc/958.htm). On January 14th 2011, EFSA launched a public consultation on a draft guidance on risk assessment concerning potential risks arising from applications of nanoscience and nanotechnologies to food and feed..

IUFoST is a federation of food science organizations linking world food scientists and technologists to promote the advancement of global food science and technology and to foster worldwide exchange of scientific knowledge. At its recent World Congress, IUFoST approved the International Society of Food Applications of Nanoscale Science (ISFANS), which is to be a global network/organization to strengthen research, communication and dissemination of information on nanotechnology applications in food (http://iufost.org/isfans).

One of OECD's strategic programmes is focused on the safety evaluation and assessment of manufactured nanomaterials to assist countries in implementing national policies to ensure responsible development of these technologies. The programme concentrates on the human health and environmental safety implications of manufactured nanomaterials, and aims to ensure that the approach to hazard, exposure and risk assessment is science-based and internationally harmonized (www.oecd.org/env/nanosafety).

1.2 Scope and organization of the conference

The conference brought together participants from developed and developing countries with different backgrounds and perspectives on nanotechnologies in food, water and agriculture – from academia, the private sector, governmental organizations, international organizations and NGOs. The conference sought to:

– identify emerging nanotechnology applications that are considered to have the greatest potential to provide broad social benefits;
– promote collaboration and partnerships among countries on issues of common interest; and
– promote a harmonized approach toward the assessment and management of potential human health and environmental risks that may be associated with the application of nanotechnologies in food and agriculture.

The Conference was organized as follows:

Morning sessions: parallel symposia covered selected themes (food packaging/sensors, food design, plant production and livestock, water and environmental applications, safety evaluation and regulatory framework) in which the state of science and technology of the various applications was discussed.

Afternoon sessions: Round tables were organized by FAO to focus on key issues of broad global interest and discuss ways for promoting the sound development of applications that contribute to solving pressing problems of sustainable agricultural development and food security.

1.3 Technical round table sessions

Three thematic areas were selected for the round tables:

1. Food "nano"-applications: ensuring broad social benefits
   (in collaboration with EFSA)
2. Nanotechnologies in agriculture: new tools for sustainable development
   (in collaboration with IUFoST)
3. Nanotechnologies: the regulatory framework
   (in collaboration with OECD).

The intent of these sessions was to provide an overview of nanotechnology applications in food and agriculture in order to gain a common understanding of the current situation, to identify emerging applications which seem to have the greatest potential to benefit both society and the environment and to develop recommendations for promoting further research and development on these emerging applications. As a preliminary, each of the panellists was asked to prepare a concise paper on a particular aspect of nanotechnologies applied to food and agriculture (see Annexes I, II and III) outlining: potential benefits; implications for human and environmental health; challenges (technical, financial and capacity); and opportunities and strategies for developing countries to gain expected benefits. In addition, the experts and participants were asked to identify and suggest possible mechanisms for overcoming identified challenges, such as partnerships and collaborations between developed and developing countries, between public and private entities and between research institutions and international organizations.

Finally, round table participants were encouraged to envisage what actions, at national and international levels, would facilitate adequate attention to and funding for applications with the greatest potential to solve problems in the agriculture, water and food sectors and promote sound scientific assessment and responsible regulation to minimize adverse effects of such applications on human health and the environment.

2. Round Table 1: Food "nano"-applications: ensuring broad social benefits

2.1 Introduction

Rapid advancements in nano-sciences and nanotechnologies in recent years have opened up new prospects in a range of sectors. The food sector, which itself is worth around US$4 trillion per annum globally, is one sector where nanotechnology applications are rapidly emerging. The main driver behind nanotechnology applications appears to be the potential for addressing a number of the current needs in the food and related sectors.

Nanotechnology applications	Food sector needs
More efficient food production	Reduction in the use of agrochemicals (fertilizers, biocides, pesticides, veterinary medicines)
More hygienic food processing, packaging, storage	Reduction in the incidence of food-borne diseases
Preservation of freshness, naturalness, wholesomeness	Reduction in the use of artificial colours, flavours, preservatives
Healthy/nutritious/tasteful products	Reduction in salt, fat and sugar intake
Improved tastes, flavours, mouth feel	Innovative, new and improved products
Functional foods for different lifestyles, and consumer groups	Improved uptake and bioavailability of nutrients/supplements
Longer shelf-life of food products	Reduction in the amount of food waste
Innovative lightweight, stronger, functional packaging	Reduction in the cost of transportation, safety and security of food products in the supply chain
Smart labels	Food authenticity, safety, traceability

The initial focus of nanotechnology applications in the food sector has been on food packaging and health-food products, with only a few applications so far in the mainstream food and beverage areas. The majority of reported applications are still in development or near-market stages. Information relating to the current scale of commercial activity in this field is patchy, which leads to wide variability in market projections. In 2006, the global market value for food and food packaging products developed using nanotechnologies was estimated by two market reports at US$4 million[2] and US$7 billion[3], and predicted for

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[2] Cientifica Report. 2006. "Nanotechnologies in the Food Industry" published August 2006. www.cientifica.com/www/details.php?id=47
[3] Helmut Kaiser Consultancy, Study: nanotechnology in food and food processing industry worldwide 2003–2006–2010–2015, 2004, available at www.hkc22.com/Nanofood.html.

growth to US$6 billion by 2012[2] and >US$20 billion by 2010.[3] According to these estimates, food packaging applications form the largest share of the current and short-term predicted market for nano-products in the food sector. The most promising areas identified for the near-future include 'Active' and 'Smart' packaging, health-foods and functional food products. Reports have also suggested that the number of companies undertaking research and development in food-related applications could be between 200 to 400,[2,4] including some major international food and beverage companies. It is widely expected that there will be many more new developments in the coming years, which could have a major impact on the food and agriculture sectors.

Market reports also suggest that the nanofood sector is currently led by the USA, followed by Japan and China, whereas Asian countries (led by China) have been predicted to be the biggest future market for nanofood products.[3] Largely because of the difference in technology development, it was considered that many developing countries may lag behind in the exploitation of new technologies.

2.2 Round-table discussion

The session started with the validation by the group of the summary table developed by Dr Chaudhry (see Annex I) in which current and projected nano-applications in the food and agriculture sectors are listed. The participants recognized the importance of having an accurate and shared understanding of the products of nanotechnologies that are already on or coming to the market.

The majority of available products fall into food packaging, and supplements/health-food/fortification areas. There is currently much research and development activity in scaling down the size of food ingredients and additives – e.g. starch, cellulose, herbs, spices – and developing nano-structured food products such as mayonnaises. Some nano-encapsulated food additives are also available, whereas the use of metal/oxide nanomaterials mainly relates to food supplement applications. Of the groups of applications identified, much of the discussion focused on the following:

1. *Water treatment*
2. *Packaging materials and bio-plastics*
3. *Nano-(bio) sensors and tracking systems*

Water treatment

Ensuring access to safe, reliable and inexpensive sources of water is one of the greatest global challenges of this century. The session extensively debated the role that nanotechnologies could play in contributing to water security, which is indeed critical to food production, food safety and food security. The panel recognized water treatment as one of the most promising nano-applications, given the various possibilities that nanotechnologies offer for water decontamination/treatment/desalination for use or re-use. Concrete examples of these applications include removal of arsenic from ground water using

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[4] Institute of Food Science and Technology Trust Fund. 2006. Nanotechnology information statement www.ifst.org/uploadedfiles/cms/store/attachments/nanotechnology.pdf.

nano-magnetite which can then be readily separated from the "cleaned" water through the application of low magnetic fields. This technology was selected by Forbes magazine as one of the top five nanotechnology breakthroughs of 2006, and is currently being tested by Rice University (Houston, Texas, USA) in a pilot-scale project in sand filters in the city of Guanajuato, Mexico.

The general idea underpinning development of accessible nanotechnologies for water purification is to take advantage of the remarkable size-dependent properties of some NPs, to develop water treatment systems that require less infrastructure and use less energy. The opportunities to exploit the properties of NPs for water treatment are numerous:

- the large surface-to-volume ratio makes some NPs superior sorbents with minimal bleed-off potential and capabilities for magnetic separation (Professor Alvarez and collaborators at Rice University are using nano-magnetite to remove As, and nZVI (Nano metallic iron) is used widely to clean up groundwater contaminated with chlorinated solvents)
- hypercatalyst dechlorinates 1000 times faster than any commercial catalyst
- membranes that incorporate nanomaterials to increase their strength and resistance to fouling (separate and destroy), etc.
- surfaces that resist biofouling and biocorrosion
- capacitive deionization to desalinate high-salinity waters
- detection and removal of pathogens, toxins

Overall, the perspectives for nanotechnology-enabled water treatment for developing countries were considered to be positive despite current barriers associated with high costs and insufficient technical capacity. Presentations during the session showed that as the market for certain applications grows, the costs can be considerably reduced and this could make them more realistic and accessible for many developing countries. These applications could support a new paradigm for water treatment: decentralized rather than central water treatment which might be expected to reduce infrastructure costs in developing countries.

In conclusion, Round Table 1 stressed the importance of capitalizing on the opportunities offered by nanotechnologies to improve and protect water quality. To do so, it was considered important to conduct pilot studies, starting with testing feasibility of approaches, such as arsenic removal, to gain momentum, and invest in outreach and education efforts. At the same time it is crucial to exercise due diligence to ensure that nanotechnologies improve material and social conditions without exceeding the ecological capital that supports them, and also to proactively assess and mitigate potential risks in the early stages of development to produce better and safer products.

Packaging materials and bio-plastics

The discussion on nano-packaging materials started with acknowledging the advantages that they may offer over existing materials, including lower weight, and better protection and preservation of foods leading to reduced wastage and lower transport costs. Some applications are already available commercially, while others are at development or market introduction stages.

With regard to packaging, coatings and films, the group recognized that there are still many questions that need to be answered due to current lack of knowledge on migration of nano-particles from packing materials to foods. The experts noted that there is an urgent need not only to generate more data on particle migration, but also on long-term exposures to NPs, even if the levels of exposure are considered to be relatively low.

Other issues that need to be addressed are the potential environmental impacts of the disposal of food packaging containing nano-particles, and of material recycling and re-use.

In the area of bio-plastics nanotechnologies create opportunities for nano-bioplastics to substitute petroleum-based plastics in the food sector. The drawbacks of using bio-plastics in this sector relate to their inferior barrier properties, lower thermal resistance and processability compared with petroleum-based alternatives. Nanotechnologies applied in the production of bio-plastics could improve the performance parameters and narrow the gap between petroleum-based packaging and bio-plastic alternatives. Such a development would promote increased use of lower carbon footprint materials for packaging and also create opportunities for developing countries to add value to natural resources. Bio-plastics can be derived from agricultural by-products or waste, thus avoiding competition for land use in food production.

With regard to costs and accessibility for developing countries, the group highlighted that food packaging applications are driven at two levels: manufacture of nano-particles and nano-structures require greater capacity and infrastructure, and thus only larger companies can sometimes invest in the necessary research and production facilities; the use/application of manufactured nano-materials, which often does not require high-tech or large investments, and can therefore be adopted by SMEs in many developing countries.

Nano-(bio) sensors and tracking systems

The ability to detect and identify pathogenic microorganisms and chemical contaminants in foods is an important component of any system that aims to ensure the safety of the food supply. Biosensors, originating from the integration of molecular biology and information technology, could provide food businesses and food safety authorities with the ability to rapidly detect or screen for pathogens and contaminants, thus improving the efficiency and effectiveness of food safety management programmes.

While at present the main demand for nano-sensors is in the medical sector, there is a growing attention to biosensors in the agri/food area to complement traditional testing and tracking methods.

The cost of using sensors in the food sector is still relatively high, but participants gave several examples of the large reduction in unit costs that are possible once the demand for a particular application grows: this should make the technologies accessible to small businesses and developing country users. Participants were of the opinion that the technology is already sufficiently advanced to develop any particular application that the market requires within about one year. Many of the sensors are robust and easy to use, making them suitable for field application. The sensors may also enable multi-analyte

detection, making quick detection of different pathogens and food contaminants a possibility. These features are particularly suitable for developing countries. Some were of the opinion that there could be reluctance on the part of some sectors of the food industry to adopt sensors indicating early food deterioration.

A question was raised concerning the environmental impact of these sensors. A future scenario with millions of nano-sensors being used would necessarily need a life-cycle impact assessment to evaluate environmental impacts. It was noted that the greatest impact is likely to derive from solvent and chemical use in the manufacture of the sensors rather than from their disposal.

With regard to traceability, the round table noted the increasing emphasis placed by official authorities and major retailers on traceability requirements. Development of specific nanomaterials and nanosensors/nanosystems may provide for new and advanced traceability tools. Nanoscale Identity Preservation is a technique that could lead to the continuous tracking of food and food "inputs", and the recording of conditions to which they are being exposed. Sensors could then be linked to recording and tracking devices using wireless and bluetooth technology. Nanosensors embedded in food packages could be used as electronic barcodes which allow traceability and tracking, combined with food spoilage markers and deterioration monitoring, thus increasing the capability of current technologies. However, in nano-tracking, loss of privacy may be of concern as nano surveillance will be able to track each step in the food chain right up to consumer.

Other considerations

Concerning mechanisms of toxicity, the panel underscored the importance of considering new uptake mechanisms such as the "Trojan horse" through which NPs, by adsorbing or binding different compounds on their surfaces, could act as carriers of potentially harmful chemicals and foreign substances into the blood, and different tissues and organs. Similarly, with regard to the use of nano-carrier systems, unintended passage of macromolecules and undigested proteins across the gastro-intestinal tract should also be considered. Some participants also noted the potential of NPs to induce allergenicity by altering protein conformation and that NPs may act as seeds for crystallization (e.g. kidney stones). However, there is no evidence of this yet and more research is needed.

Finally, another area identified to be of possible concern was the effects on gut microflora by antimicrobial NPs or nano-form celluloses used to maintain desired texture and mouthfeel in low-fat products.

3 Round Table 2. Nanotechnologies in agriculture: New tools for sustainable development

3.1 Introduction

The agriculture sector faces growing global challenges: climate change, maximizing land-use in different environments, sustainable use of resources and minimizing negative environmental impact such as accumulation of pesticides and fertilizers. The situation is further exacerbated by the need for increased food production to sustain the global population, which the UN estimates will grow from 6 to 9 billion inhabitants in the next 40 years. This rapidly evolving and yet more complex agriculture scenario sets up even more challenges in developing countries, where agriculture and commodity production are often the backbone of the economy and where commodity dependence and poverty are closely linked.

Advances in science and technologies could offer opportunities for developing countries to innovate and add value to their current commodity production systems, but can also impose additional challenges. In fact, while it is very important to support applications that could help resolve urgent problems in agriculture, it is also necessary to avoid the risk that advances in science and technology increase the disparity between developed and developing countries. Serious consideration is required with respect to the social and ethical implications of new agriculture technologies. While new agri-food technologies may make some activities more efficient in some areas, they may not necessarily solve existing problems of global food production and distribution. It is essential for developing countries to actively participate in research and development of new technologies. Strategies for capacity development in science and technology innovation and the establishment of relevant partnerships between developing countries and more technologically advanced countries must be taken into consideration.

3.2 Round-table discussion

At the beginning of the session, the participants agreed on a few premises to be used as a guide for the discussion. The group recognized that technological innovations in agriculture should be prioritized by:

- production of sufficient quantity, quality and variety of foods to feed the growing population sustainably and economically; and
- minimization of the environmental footprint linked to agricultural production.

The group acknowledged the importance of ensuring that nanotechnologies complement existing technologies and become an integral part of technological solution portfolios in order to be adapted to countries' needs and priorities.

Participants identified five main areas of nanotechnology applications where more research and work could contribute to overcoming existing challenges to sustainable agricultural development:

1. *Plant production*

2. *Animal production*
3. *Value added products*
4. *Environment*
5. *Education, communication, training*

Plant production

Precision farming in plant production is an important area of study to minimize production inputs and maximize production outputs in order to meet the increasing needs of the world population. Nanotechnologies may allow for the precise control of novel nano-agrochemicals. During the session, Dr Cui explained how most research on nanopesticides in China is focusing on the improvement of environmentally friendly properties of pesticides used in crop production. A multi-disciplinary research team led by the Chinese Academy of Agricultural Sciences is investigating a more precise and controlled delivery and release of pesticides through nanotechnology. Significant progress has been achieved in the area of nanoencapsulation and nanostructured carriers like controlled release and delivery systems for antibiotics for veterinary use (such as avermectin, ivermectin and validamycin); nanoemulsions of some fat-soluble pesticides have also been developed successfully. Mesoporous particles (such as nanoclay), activated carbon and porous hollow silica were also verified to be suitable for the controlled release and delivery carrier systems of water-soluble and fat-dispersible pesticides.

The panel highlighted the importance of field nano-sensing systems for real-time monitoring of crop growth and field conditions, including moisture level, soil fertility, temperature, crop nutrients, insects, plant diseases and weeds, to support decision-making.

Animal production

There are a number of significant challenges in animal production, including production efficiency, animal health, feed nutrition efficiency, disease control, product quality and value, by-products and waste, and environmental footprint. Nanotechnologies may offer effective, sometimes novel, solutions to these challenges.

Animal reproduction remains a challenge in both developed and developing countries. During the session, Professor Hoffman explained how his group in Brazil is working on Fixed-Time Artificial Insemination (FTAI) technology combined with nanotechnologies to effectively increase the success rate in cattle reproduction. FTAI depends on the regulation of progesterone administered through a silicone matrix. The procedure has significant drawbacks including inefficient and irregular dispersion of hormones, as well as issues related to labor intensity requiring multiple animal handlings for each attempt. Nanoscale delivery systems can significantly improve bioavailability and better control of release kinetics, reduce labour intensity, and minimize waste and discharge to the environment. Another strategy presented during the session was to monitor animal hormone levels using an implantable nano-sensing device with wireless transmission capability. In this way the information of optimal fertility period would be available in real time to assist the livestock operators.

Another critical element for sustainable animal production is the improvement of feed efficiency. Nanotechnologies may offer significant improvements here as well. As with food applications, a variety of nanoscale delivery systems have been investigated in feeds to facilitate utilization of proteins and improve the overall health of animals to maintain optimal physiological state. In addition, nanoscale delivery systems can be designed for veterinary drug delivery, which protects the drug through the gastro-intestinal tract and allows the release at the desired location for best effect. These advantages improve the efficiency by which animals utilize nutrient resources, help reduce the material and financial burden of the producers, and improve product quality and production yield.

Value added products and the environment

Nanotechnologies could improve more secure supplies for novel and healthier foods, feed, fibers and fuels, and could integrate and increase the value to be derived from utilization of animal waste and byproducts. Value-added uses through bioconversion of animal waste into energy and electricity will result in renewable energy and high-quality organic fertilizer. However, some of the participants in this round table expressed concern about the use of bio-based energy, since promoting this type of energy could increase the pressure to generate "waste", thus creating competition among agricultural products and in land use. Current research has been focusing on low-value biomass to avoid competing with food uses and significantly improve bioconversion efficiency for better utilization of biomaterials. It was also noted that nanotechnologies used in agriculture could result in reduced agricultural biodiversity by supporting mono-crop agriculture. In addition, nano-agrochemicals and farm inputs may present new threats to health and safety.

The discussion also focused on the possibilities for renewable energy to be used in post-harvest operations such as drying, storage and preservation of agricultural products. Inexpensive types of solar-powered electricity have long been an aspiration for many countries, and nanotechnology-based photovoltaic energy is currently a high research priority worldwide. Other nanotechnologies for solar energy conversion to electricity and for energy storage are also active areas of research and development. However, many obstacles still need to be overcome in order to improve efficiency, reduce costs and make these applications feasible and affordable for developing countries.

Roundtable participants discussed areas where more research is needed:

- New generation of photovoltaic cells with increased efficiency using quantum dots and carbon nano-tubes
- Catalytic NPs coatings that could increase the efficiency of electrolysis
- NPs coatings that could eliminate the need for expensive metals like platinum in hydrogen fuel cells and thus reduce costs
- Development of highly efficient supercapacitors based on nanomaterials
- Tuning of nano-rods to absorb various wavelengths of light, which could increase the efficiency of the solar cell because more of the incident light could be utilized

Education, communication, training

The issues identified and discussed with respect to education, communication and training were relevant to the entire Conference, and are addressed in the Conclusions (see Section 5, below).

4 Round Table 3. Nanotechnologies: The regulatory framework

4.1 Introduction

The introduction of nanotechnology applications in the food and agriculture sectors and their acceptance by consumers will largely depend on how confident people feel that regulatory systems are effective in protecting them against potential risks. The application and use of nanotechnologies should imply a high level of public health protection and consumer safety, as well as protection of the environment. The regulatory challenge is therefore to ensure that society can benefit from novel applications of nanotechnologies, while appropriate levels of health, safety and environmental protection are maintained.

A reliable and stable regulatory framework is essential for the food industry to fully exploit the advances and potential of nanotechnologies. However, due to the wide diversity of potential food and agriculture applications of nanotechnologies, the unique and novel properties of nanoparticles, and the existing scientific uncertainties about nanotechnologies, there are a number of challenges that regulatory frameworks need to confront in order to ensure a sound and effective governance of these new technologies.

4.2 Round-table discussion

Discussions during Round Tables 1 and 2 identified some of the regulatory issues relevant to nanotechnologies. These were further debated and expanded during Round Table 3.

Partcipants recognized that a number of challenges need to be overcome to ensure the effective regulation of food products developed using nanotechnologies and to promote a harmonized approach among countries for regulating these products. The main challenges relate to

- risk/safety assessment of NPs (data requirements for approval processes);
- terminology and definitions related to nanotechnologies and implications for regulation and labeling; and
- *challenges to enforcement.*

Risk/safety assessment of NPs (data requirements for pre-market approval)

Existing risk assessment principles and methodologies are generally appropriate for engineered nanomaterials, but the participants expressed the need for clearer guidance on safety testing methods and for more exposure assessment data due to the limited knowledge of the human health effects of NPs. Participants encouraged a more coordinated approach at the international level among the various international organizations (e.g. FAO, OECD, WHO) and other agencies, such us EFSA, that are working on a tiered approach for risk assessments of categories of NPs and on the development of a decision-tree to guide risk assessment processes. This approach will proceed on the basis of weight of evidence. The work carried out by Professor Oberdörster and his group in prioritizing NPs on the basis of risks (benchmarking NPs) is moving towards this direction and was presented during the session.

As the physico-chemical properties of NPs vary widely, and because of the impact of such properties on biological/toxicological effects of NPs, one high priority is to establish predictive toxicity testing methods in order to characterize a potential hazard of the rapidly increasing numbers of new NPs. Conceptually, it would be helpful to express the biological/toxicological activity of NPs relative to that of benchmark (BM) or reference NPs (Ref NPs) that have already undergone rigorous testing and were found to be either of low toxicity ("negative" benchmark or reference) or of very high toxicity ("positive" benchmark or reference). These BM or Ref NPs could serve to rank NPs of unknown toxicity and thereby provide necessary information for the first step of the risk assessment process, i.e. Hazard Identification. Important for the establishment of BM/Ref NPs is the use of *in vitro* tests that have been validated by realistic *in vivo* assays, involving assessment of responses over a wide range of doses and a careful analysis of the resulting dose-response data. An example based on the use of specific dose- and response-metrics is described by Rushton et al. (2010),[5] which will allow a Hazard Scale for NPs to be generated based on the highest reactivity (or effect) per unit surface area. Validation is essential, so that the use of validated *in vitro* assays can be utilized to evaluate large numbers of different types of NPs with respect to their ranking against the BM or Ref NPs. This information, coupled with knowledge about human exposure, may be applied to perform a full risk assessment. However, the group recognized that exposure assessments of NPs toxicokinetics are still largely missing.

On the safety requirements to enter the market, the group reaffirmed the key principle that only safe food should be on the market and that the responsibility of ensuring that food is safe lies primarily with the industry. When this concept is applied to nanotechnologies, the first obstacle is related to the uncertainty of the data required for entering the market. On this issue, the group strongly expressed the need for clearer articulation of data requirements for approval processes as well as the need for an international database, accessible by all countries, in which all relevant data and official information on different national and regional requirements for accessing the market are collated. The group also agreed on the need to re-evaluate approved products if they are redesigned in nano-form (food additives, vitamins and minerals); post-market surveillance should also take place to ensure that potential long-term toxic effects are monitored as well.

Terminology and definitions related to nanotechnologies and implications for regulation and labeling

In the discussions, some experts supported the idea that even in the absence of agreed definitions for nano-particles, nanostructures etc., regulatory frameworks can still capture and therefore regulate nanotechnology applications. However, having internationally agreed working definitions would be necessary to provide information and communicate on nano-related issues, including labelling of nano-products. Other experts reiterated the need for agreed definitions for the purpose of regulating nanotechnologies. Some experts also expressed the request to international organizations that are already working on the development of nano-definitions (e.g. International Organization for Standardization

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[5] Rushton EK, Jiang J, Leonard SS, Eberly S, Castranova V, Biswas P, Elder A, Han X, Gelein R, Finkelstein J and G. Oberdörster. Concept of assessing nanoparticle hazards considering nanoparticle dosemetric and chemical/biological response metrics. J Toxicol Environ Health A. 73(5):445-61; 2010.

Technical Committee (ISO/TC) 229 Nanotecnologies) to work together on a glossary of terms for nanotechnologies

With regard to labelling, the group agreed on the importance of ensuring openness and transparency for consumers in order to allow them to make informed choices. In this regard, it would be important to have more discussion on labelling of foods that have been manufactured using nanotechnologies or that contain novel NPs, and to find the right way to balance consumers' right to know what is in a product and the risk of reducing consumer choice if products are taken off the market due to the unwillingness of retailers to have labelled products.

Challenges to enforcement

One of the most urgent challenges identified in relation to the enforcement of a regulatory framework is the lack of routine detection methods of NPs in foods. The group suggested that the industries and producers need to strongly commit to the development of suitable detection methods, but that in the absence of such methods it would be necessary to use existing traceability systems to track and monitor NPs along the food chain.

The group also recognized that the existing regulatory uncertainties could bring additional challenges to SMEs, as they might be not able to invest in order to comply with the regulatory approval process. At the same time, building up efficient regulatory systems capable of assessing, tracking and monitoring nanotechnologies in food and agriculture can be very costly. Many countries lack the infrastructure, funds and capacity to set up and implement such systems. While the group recognized that it would be very difficult to achieve a universal regulation, and decisions need to be taken at the local/regional level, participants also agreed on the usefulness of partnerships between national and regional authorities in order to mutually recognize risk assessments.

5 Conclusions

The round-table discussions concluded that nanotechnologies could potentially address global challenges in food and agriculture, but also recognized that they may also involve issues of global relevance requiring internationally shared vision and a common strategy for moving forward.

The participants emphasized the responsibility of the scientific community to regard nanotechnologies as a tool for sustainability, rather than as either a panacea or a new challenge to public and environmental health. This responsibility imposes a proactive approach to risk assessment; however, review of the current nanotechnology literature indicates unbalanced investment in research into the development of applications, when compared with research into public health and the environmental implications of these applications. However, at the same time it is worth mentioning that there are positive signs that this situation in funding may change; as one example, the Brazilian Coordination for Development of Graduate Human Resources (CAPES is supporting and sponsoring 38 programmes on nanotechnology for a total of **approximately US$40 million, of which** one-third is related to human health and one-third to risks involved in and safe use of nanotechnologies.

At the international level, OECD has done extensive work on identifying environmental and human health research gaps.[6] Furthermore, the OECD's Sponsorship Programme on the Testing on Manufactured Nanomaterials is currently testing 13 manufactured nanomaterials of commercial relevance (for example, silicon dioxide, titanium dioxide, carbon nanotubes, silver) for approximately 60 endpoints relevant to environment and human health safety[7] in order to understand their intrinsic properties.

The round tables also agreed that it is essential, first of all, to clearly understand the problems, causes of problems, real needs and capacities in developing countries, and not develop and offer "quick fix" technological solutions that could do more harm than good in the end. Thus research and development must examine technological solutions that build on local knowledge and capacities, rather than displacing or marginalizing them. Public investment should go into publicly available technologies (non-patented, published work), and funds should be made available to develop local capacity in order to make decisions within international architecture to cope with global dimensions and challenges. It is also very important to prioritize investments and research in applications that aim to improve food security and safety, and environmental health. Such prioritization requires a multidisciplinary approach and cross-sectoral collaboration within and between academic researchers and industry. In this regard, participants also considered that the main innovation route to nanotechnology applications would possibly arise from SMEs and small spin-off companies. Therefore, spin-off companies need to be encouraged to work in this field – especially in the developing countries; and collaboration within a country between different research institutions, industry and government departments should be promoted.

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[6] See www.oecd.org/env/nanosafety/database.

[7] Nanomaterial identification, physical-chemical properties and material characterization, environmental fate and environmental toxicology, mammalian toxicology and material safety. More about this programme can be found at www.oecd.org/env/nanosafety.

The participants encouraged the establishment of an international platform under the coordination of international organizations (e.g. FAO, OECD, UNESCO, WHO), where collaborations and partnerships be promoted in priority areas, such as food safety and water. It will be critical to work together for technological solutions that build on local knowledge and capacities, ensure additionality and complement existing technologies. Efforts should be made to improve technical capacity and competence in developing countries. The group also expressed the need for education and training programmes on nanotechnology that not only deal with scientific and technical aspects but also social sciences, to ensure that the ethical implications of nanotechnologies are also addressed. The sessions stressed the importance of public sector engagement and the need for more resources and efforts to be devoted to education programmes. Participants indicated the need for the development and maintenance of publicly available materials, information and training modules to ensure relevance and currency via online resource database and libraries. Participants emphasized the need for increased support to science and agricultural literacy by engaging with journalists and informal education (e.g. media, museums) to communicate nano-related issues to the public.

Future directions

Various mechanisms to move forward were identified, including the use of training programmes and extension services to conduct research on nano-applications and their use. Participants emphasized the importance of having dedicated sessions at international conferences in order for information and knowledge on nanotechnologies to be quickly disseminated to interested parties.

On the basis of the three-day discussions, it was recommended that:

- international organizations (i.e. FAO, WHO, UNESCO, etc.) work together to create an open-access database or portal on the application of nanotechnologies in food and agriculture, including information on market access requirements in different countries;

- international organizations form a multi-stakeholder oversight group to support public sector engagement in nanotechnologies;

- international organizations develop an international exchange platform for sharing and discussing information on nanotechnology issues of global relevance;

- FAO and collaborating organizations act as facilitators for developing partnerships and collaborations among countries; and

- FAO work together with other organizations (e.g. EFSA, OECD, WHO) to review and develop an internationally accepted tiered approach for risk assessment of NPs.

This conference served as a solid starting point for future initiatives and collaborations. Partnerships and collaborations on key areas of sustainable development emerged during the intense conference discussions. The following are only a few examples of potential future activities for which foundations were laid during NANOAGRI 2010.

- Initial arrangements have been made for a series of potential collaborations on nanotechnology applications for water purification among research institutes, universities and international organizations.

- The long-standing collaboration between Brazil and the United States on nanotechnologies was further strengthened during the conference, and new proposals on nano-biopolymers are currently under discussion.

- Members of the trilateral developmental initiative between India, Brazil and South Africa had the opportunity to explore opportunities for new projects on nanotechnologies in food and agriculture.

- Exchanges between PhD students and Post Doctoral students among developed and developing countries were proposed and are currently being finalized.

The next conference has been tentatively scheduled for 2012 to be held in Brazil, in collaboration with IUFoST. Efforts will be made to ensure even broader participation from developing countries.

Annex I
Round Table 1 background paper and related mini papers

Round table 1
Background paper
Food "nano"-applications: ensuring broad social benefits
Rickey Yada, Charity Parr-Vasquez, David Carlander, Hongda Chen

Table of Contents

1 Introduction

Science and technology at the nanoscale promises to be among the most revolutionary scientific fields in decades. It has been marked as having the potential to provide many novel solutions to both emerging and existing global problems such as energy production, and food and clean water shortages. This article is a brief review of the current state, future directions and safety/consumer/public issues of potential uses of nanotechnologies in the food sector.

Science and technology at the nanoscale level, i.e., "nanotechnology", is generally defined as any technology that deals with objects within the range from 1 to approximately 100 nm when those objects, in addition to their small size, exhibits properties and phenomena not seen at a larger scale of the same materials. Various definitions sometimes also includes connotation wording that includes the intentional aspect of creating a nanomaterial, i.e. that there is an underlying thought and technological possibility to create the desired size and characteristics (e.g. engineered or manufactured).
"Natural" nanomaterials are usually excluded in the discussion of "nanotechnology" as are most biological processes, e.g., synthesis of proteins, which take place at the nanoscale level. Several proposals for definitions are discussed in various national and international settings, but an agreed definition is yet to evolve. The need for an enforceable definition is often raised by regulatory bodies, and currently this is frequently based on size (or metrics derived from size such as specific surface area).

Nanotechnology is considered by some food scientists and technologists as not a new field. For example, in the process of cheese making casein micelle stability is altered by the cleavage of a milk protein, k-casein. This process appears to fit part of the general nano definition; i.e. nanoscale phenomenon, novel protein structure and property changes and action at atomic precision. However, this excludes the engineered (or manufactured) aspects of creating the desired substance or properties as historically the altered micelle stability is achieved by natural processes that have not been intentionally engineered or manufactured to give rise to the desired effects. The mechanistic understanding of many natural processes has been elucidated and made possible by applying methods and instrumentation now used to intentionally create engineered/manufactured nanoparticles. Natural processed food structures at the nanoscale would thus not fall under the general understanding of the definition.

To many, nanomaterials are difficult to visualize, and therefore, a visual aid is often used to relate size to objects (Fig. 1). In this light, the evolution of nanotechnology is largely attributed to the development of instruments and tools, such as transmission electron, atomic force and scanning tunnelling microscopes which has allowed researchers to visualize and control objects with precision that could only be previously theorized.
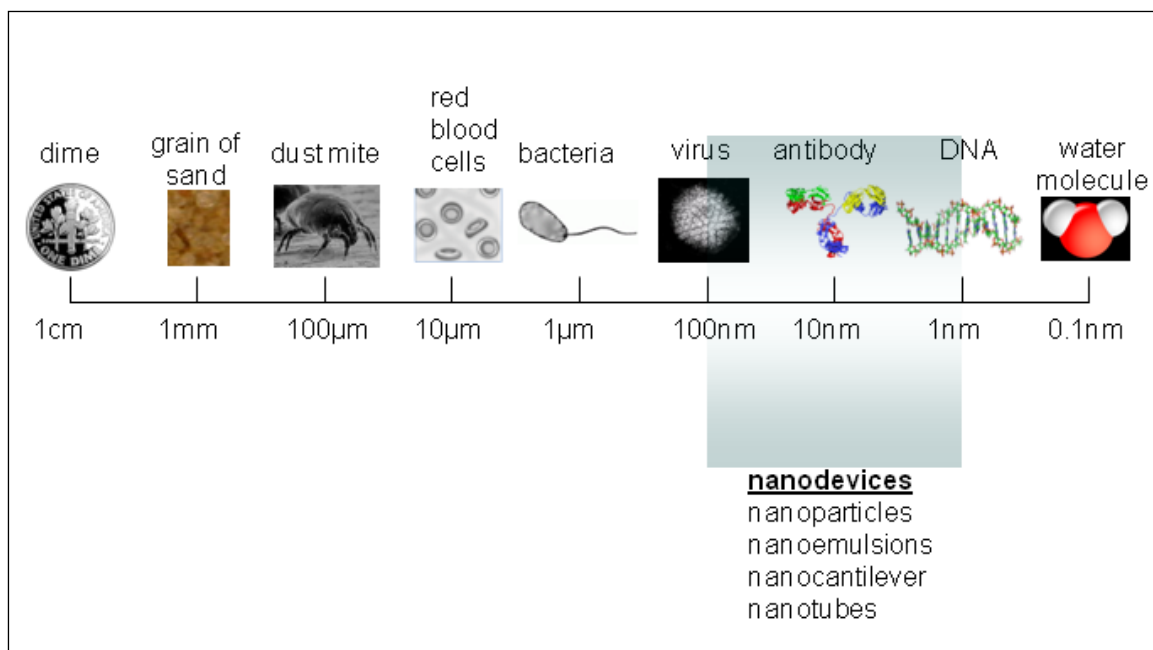
Figure 1. A visual displace of object that fall into the nano and micro size ranges

Nanotechnology allows for the possibility to control and modify material and systems at the nanoscale level to produce altered characteristics that may differ considerably from those at present at larger scale. For example, one of those characteristics is the increase in surface area of nanoparticles. This increase has the possibility of rendering nanosized materials more reactive (as more atoms with possibilities to react will be present on the surface), and the small size may allow the nanoparticles to pass through biological membranes and as a consequence be transported via biological systems (e.g. blood and lymph) to locations other than the initial portal of entry (for food, the passing over the intestinal membranes). However, as with all new technologies, it is the potentially new and unique properties that give rise to the need for safety assessment/evaluation and risk/benefit analysis to ensure that human health and safety as well as environmental and public concerns are addressed.

1.1 Interactions of nanomaterial in the food

There are several possible interactions that may take place between nanomaterials and the food (Simon, 2008). Nanomaterials are often not present as primary (individual free) particles, but occur in agglomerated (weakly connected) or aggregated states (more strongly bound together).

Nanomaterials may interact with food constituents, such as protein, lipids, carbohydrates nucleic acids and other biomolecules (e.g. flavours, pigments, vitamins, preservatives). Nanomaterial characteristics and properties are influenced by the surrounding environment (e.g. pH, ionic strength, presence of surfactants, proteins, and other types of surface modifications) and the nanomaterial interaction with various types of food constituents has the potential to alter the properties of the food constituents.

2 Applications of nanotechnologies in the food sector

As with many other disciplines, the potential applications of nanotechnologies to food science are emerging. It is predicted that the economic value of nanoscale science and technology on the agri-food market is expected to be $20.4 billion in 2010 (Farhang, 2009). Nanotechnologies has the potential to benefit product development (e.g. delivery, formulation and packaging), food processing (e.g. nano-capsules, nano-powders, nano-ingredients), and food safety (e.g. nano-sensors and nano-tracers) (For review see Chaudhry, 2008).

See ANNEX I for complete list of current and projected nanotechnology applications in the food and agriculture sectors.

2.1 Food packaging

Much attention has been focused on the potential use of nanotechnology to produce food packaging that will not only improve product safety but also improve and/or maintain the quality. The use of nanomaterials will allow for the production of packaging materials with increased mechanical strength, conductivity and functionality as compared to their traditional counterparts (Azeredo *et al.,* 2009; Alexandre *et al*., 2001; Brody, 2006; Brody *et al*., 2008; Darder *et al*., 2007; Deshmukh, 2006). New functionalities can arise from the incorporation of nanomaterials that has an active role in the packaging material (such as antimicrobial or oxygen scavenging properties), or nanomaterials with sensors that can monitor the condition of the food (e.g. freshness, storage temperature, microbial contamination).

The term nanocomposites are often used to describe systems in which nanoparticles are dispersed in a continuous polymer matrix. These nanocomposites are considered superior in that they enhance thermal stability, mechanical strength, conductivity and gas barrier properties without jeopardizing toughness (Alexandre and Dubois, 2000) and optical transparency (Wan *et al.,* 2003). Much research has been undertaken on nanocomposites that consist of a combination of clay and a polymer. For example, commercially modified montmorillonite (MMT) clay is used in nanocomposite production as an additive to improve gas permeability, and mechanical properties (Lagaron *et al*., 2004) to produce a plastic product that is lighter than the traditional counterpart (Brody, 2006; Brody *et al*., 2008); however, this desired characteristic often gives rise to additional problems when it comes to rigidity, permeability or resistance to water. Research is currently being conducted to examine the addition of certain nanomaterials to overcome these drawbacks while still maintaining biodegradability (Avella *et al*., 2005).

Presently, studies are being undertaken to also looking to nanoscience to generate 'smart' packaging (For review see Dunn 2004). Presently, scientists have developed 'smart' packages that contain oxygen sensors which are composed of ink that contains nano-particles of titanium dioxide. The nano-particles become sensitive to oxygen levels once they are exposed to UV light, changing colour as oxygen levels are altered providing an indication of the integrity of the product package during storage (Dunn 2004).

2.2 Applications for food processing

Nanotechnology has the potential to substantially alter both the physical and functional properties of the foods we eat. It is now conceivable that food scientists can develop 'smart' foods that will respond to the body's nutrient deficiencies and deliver nutrients more efficiently without altering the taste or texture of the product. Table 1 identifies some of the products available on the market that have been impacted by nanoscience advances (The project on emerging nanotechnologies, 2009).

Table 1- Nano-products currently on the market (adapted from "The project on emerging nanotechnologies", 2009)

Company	Product Name	Functionality
Tip Top®	Tip Top UP® Omega-3 DHA	Fortified with nanocapsules containing Omega-3 DHA rich tuna fish oil
Shemen industries	Canola Activa oil	Fortified with nonesterified phytosterols encapsulated via a new nanoencapsulation technology (NSSL: Nano-sized self assembled liquid structures, developed by Nutralease (Israel) for optimizing the absorption and bioavailability of target nutrients
RBC Life Sciences®, Inc.	Nanoceuticals™ Slim Shake Chocolate	Nanoscale ingredients that scavenge more free radicals, increase hydration, balance the body's pH, reduce lactic acid during exercise, reduce the surface tension of foods and supplements to increase wetness and absorption of nutrients
Shenzhen Become Industry & Trade Co., Ltd.	Nanotea	Nano-fine powder produced using nanotechnologies.
Aquanova	NovaSOL Sustain	nano-carrier that introduces CoQ1O to address fat reduction and alpha-lipoic acid for satiety

2.3 Applications for improved food safety

The global incidence of food borne illnesses is difficult to measure however, it is estimated that roughly 2 million people die from diarrhoeal diseases, largely attributed to contaminated food and water, annually (WHO, 2004). Proper hygiene, storage and packaging are the most important to factors to alleviate these numbers by improving the safety and wholesomeness of food products.

Nanotechnologies may beneficially contribute to food safety. For example, the incorporation of sensors to detect microbial contamination or to increase shelf life by reducing the presence of oxygen. Nanotechnology may allow for systems that are less cumbersome, more

portable, have increased sensitivity and reduce detection time, and technical training of personnel necessary to conduct pathogen detection.

3   Assessing potential risks of Nanotechnologies

Currently, many nations (USA, Canada, the European Union, Australia, New Zealand, Japan and China) have issued policies and position statements with regards to the use of nanotechnologies. Risk assessment/evaluation and regulatory bodies have all identified the need for additional data and increased understanding when it comes to environmental health and safety impacts and implications (EHS) of nano-products (see Round Table 3 background paper; Bugusu *et al.,* 2009).

A prerequisite for foods is that they are safe to consume, therefore, several steps must be taken to ensure safety before products are introduced to the market place (Sandoval, 2009). Consumer concerns often arise due to lack of openness and transparency from industry, regulators and risk assessors, understanding of the technology and of the potential personal benefits and risks. Achieving the confidence and trust of consumers is a complex process. Generation of unique and specialized risk assessment and management systems in addition to defined regulations will hopefully alleviate some of the consumer fears that typically emerge with the introduction of new technologies.

Risk assessments of new products must be undertaken to identify potential hazards to human health and appropriate risk assessment and management strategies must be adopted (The Royal Society of Science, 2004; Council of Canadian Academies, 2008; EFSA, 2009; FAO/WHO, 2009; Bouwmeester 2009). The traditional risk assessment comprises four stages; hazard identification, hazard characterization, exposure assessment and risk characterization (FAO/WHO, 1995, 1997; SSC, 2000; CODEX, 2007). Health risk is defined as the combination of the probability of occurrence of harm to health and the severity of that harm. This risk assessment approach is considered an appropriate starting point to address the additional safety concerns that may arise due to the specific characteristics that arise in the nano scale region (EFSA, 2009).

In addition to the direct assessment of the various products, the possibility and the consequences of a failure of a nanomaterial to deliver its intended functionality should be considered. The failure of a nano sensor that monitors microbial growth or the presence of allergens could have severe health consequences. The increase bioavailability that may arise as a consequence of making a nutrient in the nano size range should be assessed to avoid excessive intake which may have deleterious effects on the nutritional status. Such effects may need to be mitigated by revised recommended daily intakes.

Furthermore, in an increasingly environmentally savvy society, in addition to the traditional food safety assessment, environmental impacts must be studied and addressed as well. It was recently advocated by both American and European participants that life cycle considerations must be taken to assess the true environmental viability of nano-products (Sandoval, 2009). Determining the environmental impact of nano-product will include exposure assessment, hazard identification and characterization of manufactured

nanomaterials, ecotoxicology of manufactured nanomaterials; investigation of the feasibility to extrapolate manufactured nanomaterial toxicity using existing particle and fibre toxicological databases; environmental and biological fate, transport, persistence, and transformation of manufactured nanoparticles; and recyclability and overall sustainability of manufactured nanomaterials (For review see Dreher 2004 and Sandoval, 2009).

The potential impacts of applications of nanotechnologies in the food sector are likely to be profound, beneficial and far reaching if its implementation and application in society is done under responsible governance that carefully considers in addition to the basic health and safety aspects the ethical, legal and societal impacts (ELSI) and values, which would aid in establishing the public's trust. In addition, consumer education will be of particular importance in explaining the possibilities nanotechnologies offers, as with any new technologies. Developing and maintaining the credibility of nanoscience will require a multi-disciplinary approach, where the industry and scientific communities coordinate a rational approach to establishing nanotechnology as a viable publically accepted science of the future.

4 Concluding Remarks

The intent of this backgrounder is to provide an overview of food "nano" applications in order to share common understanding of the current situation around the topic and to base recommendations and strategies for moving forward on the best scientific knowledge presently available.

During the roundtable sessions, participants and participants will be asked to identify: potential benefits; implications for human and environmental health; challenges (including technical, financial and capacity-related challenges); as well as opportunities and strategies for developing countries to gain the expected benefits. In addition to this identification process, it is important that the participants and participants also identify and suggest possible mechanisms for partnerships and collaborations (e.g. between developed and developing countries, public-private, between research institutions and international organizations etc), which will be incorporated into the final report of this event.

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31. UK The Royal Society and The Royal Academy of Engineering. 2004. Nanoscience and nanotechnologies: Opportunities and uncertainties. July 2004, 1-127. http://www.nanotec.org.uk/report/Nano%20report%202004%20fin.pdf

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

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
Development of nanostructured* food products * also termed as nanotextured	Processed food nano-structures	Novel or improved tastes, flavours, textures	Use of less fat, better tasting food products, more stable emulsions. A typical product of this technology would be a nanotextured food (e.g. ice cream, mayonnaise, spread, etc.) which is low-fat but as "creamy" as the full-fat alternative. Such products would offer a 'healthy' option to the consumer.	Ingestion via food/drinks.	Currently, there is no clear example of a commercially available food product that is proclaimed to have been specifically nanostructured, although development of microemulsions is known to generate a range of droplet sizes – some in the nano range. A few nano-structured food additives are understood to be in the R&D pipeline – some may be near market.	One example, currently under R&D, is that of a mayonnaise which is composed of an emulsion that contains nanodroplets of water inside. The mayonnaise would offer taste and texture attributes similar to the full fat equivalent, but with a substantial reduction in the fat intake of the consumer.[8] Processing foodstuffs at submicron or nano scale is also known to kill any microbial pathogens.
Nano-Carrier systems for delivery of	Nano-carrier systems in the form of liposomes or	Taste masking of some ingredients and additives	Preservation of ingredients and additives during	Ingestion via food/drinks.	A number of nano-carrier based substances are	The increased absorption, uptake and improved

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
nutrients and supplements	biopolymer-based nanoencapsulated substances – e.g. supplements and nutraceuticals for food and beverage products.	such as fish oils, or protection of ingredients from degradation during processing. Also claimed for improved optical appearance, and improved bioavailability of nutrients/supplements, antimicrobial action, and other health benefits.	processing and storage, masking unpleasant tastes and flavours, controlling the release of additives, as well as enhanced uptake of the encapsulated nutrients and supplements.		available; for example, food additives (benzoic acid, citric acid, ascorbic acid), and food supplements (vitamins A and E, isoflavones, ß-carotene, lycopene, lutein, omega-3 fatty acids, coenzyme-Q10) etc.	bioavailability of certain additives and supplements may also alter tissue distribution of the substances in the body. ADME properties of some encapsulated substances may become different from conventional bulk equivalents.
Organic nanosized additives for food, health food supplements, and animal feed applications	Organic additives (many of them naturally occurring substances) manufactured in the nanosize range.	Due to larger surface area, lower amounts would be needed for a function, or a taste attribute.	The main claimed benefits include better dispersibility of water-insoluble additives in food products without the use of additional fat or	Ingestion via food/drinks.	A range of additives and food/feed products is available. Examples include ongoing R&D in Taiwan[9] and Japan[10] into micronized starch, cellulose, wheat, rice, and a range of herbs	This type of application is expected to exploit a much larger segment of the food and health food sectors. The materials range from colours, preservatives, flavourings, to supplements and

[9] Hwang, L.S. and Yeh, An-I. (2010) Applying Nanotechnology in Food in Taiwan, Paper presented at the International Conference on Food Applications of Nanoscale Science (ICOFANS), Tokyo, Japan, 9-11 June 2010.

[10] Tsukamoto, K., Wakayama, J and Sugiyama, S. (2010) Nanobiotechnology approach for food and food related fields, Poster presented at the International Conference on Food Applications of Nanoscale Science (ICOFANS), Tokyo, Japan, 9-11 June 2010.

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
			surfactants, and enhanced tastes and flavours due to enlarged surface areas of the nano-sized additives compared with conventional bulk forms. Virtually all products in this category are also claimed for enhanced absorption and improved bioavailability in the body compared to conventional bulk equivalents.		and spices for food applications such as turmeric.	antimicrobials. Several products containing nanosized additives are available in the food and health food sectors. Examples include vitamins, colorants, flavoring agents, antioxidants and other nutraceuticals.
Inorganic nanosized additives for food, health food and feed applications	Inorganic additives and supplements manufactured in the nanosize range	Due to larger surface areas, the nano-sized additives would need relatively smaller amounts for a function, or a taste attribute,	Enhanced tastes and flavours due to enlarged surface areas of the nanosized additives over conventional forms. Food and	Ingestion via food/drinks, and potential bioaccumulation in the body.	A range of inorganic additives is available in the supplements, nutraceuticals, and food, feed and health food sectors. Examples include inorganic materials	Some inorganic additives in this category may contain insoluble, indigestible and potentially biopersistent nanoparticles.

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
		compared to bulk equivalents. Other projected benefits include increased hygiene due to antimicrobial activity.	feed supplements in this category are also claimed for enhanced absorption and improved bioavailability compared with conventional equivalents.		(alkaline earth metals, non-metals, and surface functionalized materials), such as silver, iron, silica, titanium dioxide, selenium, calcium, magnesium, platinum etc.	
Food packaging applications	Plastic polymers containing (or coated with) nanomaterials for improved mechanical or functional properties.	Improved mechanical and functional properties of polymers used as food contact materials (FCMs) or in food packaging.	"Improved" FCMs in terms of flexibility, gas barrier properties and temperature/moisture stability. "Active" FCMs incorporating metal/metal oxide nanoparticles (e.g. silver, zinc oxide, magnesium oxide) for antimicrobial properties. They are claimed	Through (potential) migration into foodstuffs, or ingestion of edible coatings.	Examples include plastic polymers with nanoclay as gas barrier, nanosilver and nanozinc oxide for antimicrobial action, nanotitanium dioxide for UV protection in transparent plastics, nanotitanium nitride for mechanical strength and as a processing aid.	This area of application constitutes the largest share of the current and short-term predicted market for nanotechnology applications in the food sector. Migration studies, and modeling assessments, have so far shown little evidence of potential migration of nanoparticles from plastic polymers into food. Bio-polymer based nano-composites may

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
			to prevent microbial growth on the surface of plastic packaging and hence keep the packaged food fresher over relatively longer periods. Another application is the deposition of metallic aluminium on plastic films.			behave differently – but have not been studied in detail.
Nanocoatings on food contact surfaces	Nanoscale coating.	Nanocoatings for FCMs with barrier or antimicrobial properties.	For "active" or self-cleaning surfaces in food processing facilities such as abattoirs.	Through potential migration into foodstuffs.	A number of nanomaterial-based coatings are available for food preparation surfaces, and for coating food preparation machinery. Examples include nanosilica coating for hydrophobic surfaces; titanium dioxide or zinc oxide nanocoating for photocatalytic sterilization of food contact surfaces, and	Nano-coatings of silica and titanium dioxide have been used for self-cleaning surfaces. Silver nano-coatings have been used for antimicrobial activity to maintain hygienic environment. Also reported are nanoscale lipid structures for development of water-repellent surfaces.

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
					nanocoating of silver for hygienic food preparation surfaces.	
Surface functionalized nanomaterials	The 2nd generation nanomaterials that add certain functionality to the matrix, such as antimicrobial activity, or a preservative action, such as through absorption of oxygen.	For food packaging materials, functionalized ENMs are used to bind with the polymer matrix to offer mechanical strength or a barrier against movement of gases or volatile components (such as flavours) or moisture.	Processing aids, additives for food preservation/detoxification Antimicrobial and other health benefits.	Through potential migration into foodstuffs.	Main uses are currently in food packaging, possible uses are also emerging in animal feed. Other examples are not yet available, but a number of nano-bio materials are under development – some may find use in food related applications	Examples include organically modified nanoclays that are currently used in food packaging to enhance gas-barrier properties. As nanotechnologies converge with other technologies (e.g. biotechnology), the use of functionalized nanomaterials in food and related applications is likely to grow in the future.
Nanofiltration	Filtration products based on porous silica, regenerated cellulose membranes.	Filtration of undesired components in food – such as bitter taste in some plant extracts, and clarifying wines and beers. Also used for water filtration.	Potential removal from food of undesirable tastes, flavors, toxins, etc. Removal of insoluble suspended matter from beers and wines,	Ingestion via food/drinks.

Potential exposure only if silica nanoparticles get into the filtered products. | Colloidal silica (thought to be in micro-sized agglomerated form) is known to be used in clarifying beers and wines. | The use of porous silica in nano-filtration systems needs to be considered differently from the use of free nanoparticles or their agglomerates in food products. |

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
			water filtration.			
Nanosized agrochemicals	Nanosized fertilizers, pesticides, veterinary drugs	Controlled application/release of agrochemicals.	Improved delivery of agrochemicals in the field, better efficacy, better control of application/dose, less use of solvents in agricultural spraying.	Potential risk of worker exposure to hazardous substances, consumer exposure through potential carry-over of residues in foodstuffs.	Despite known R&D activity in this area, there is no product available on the market at present. Nano-encapsulated and solid lipid nanoparticles have been explored for the delivery of agrochemicals, such as slow- or controlled-release fertilizers and pesticides. One reported example is a combined fertilizer and pesticide formulation encapsulated in nanoclay for slow release of growth stimulants and biocontrol agents.	Any application for pesticide or veterinary medicine will need pre-market approval.
Nanosensors for food labeling	Incorporation of nanomaterials into intelligent inks (that respond to a change in the	Nano(bio)sensors that can monitor condition of the food during transportation	Better food authenticity, safety and security from the use of "Smart"	Through (potential) migration into foodstuffs.	A few labels are already available, many other are understood to be under development. This area	Of particular interest in this regard are the safety and quality indicators that can be applied as labels or

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
	condition of packaged food) to print labels that can indicate safety and security of the packaged foodstuffs.	and storage. Nanobarcodes can be incorporated in food packaging to enable verification of product authenticity.	packaging, which incorporate nanosized sensors that can monitor condition of the food during transportation and storage. Also under development are "Intelligent" packaging concepts that will release a food preservative only when releases preservatives only when triggered by rough handling or transport abuse, or when microbial activity initiates in the packaged food.		of application is likely to see a rapid growth in the future.	coatings to add an intelligent function to food packaging. For example, to monitor the integrity of the packages sealed under vacuum or inert atmosphere by detecting leaks, freeze–thaw–refreeze scenarios by detecting variations in time–temperature, or microbial safety by detecting the deterioration of foodstuffs. R&D work also is ongoing to integrate nano(bio)sensors with Radio Frequency Identification Display (RFID) systems to enable tracking down of food products in the supply chain.
Water decontamination	Nano-iron, other photocatalysts (e.g. titanium dioxide) may also be used.	Water treatment	Breakdown of organic pollutants, oxidation of	Consumption of treated drinking water, or carry over from wastewaters used in	Nano-iron produced and available in industrial scale quantities.	A number of companies are thought to be using the technology in

Application	Nanotechnology	Function	Potential benefits	Possible routes of human exposure	Availability on the market	Comments
			heavy metals, elimination of pathogens.	agriculture and food production.		developing countries where water resources are scarce.
Other applications	Different nanomaterials	Animal feed	Reduced use of feed additives, improved bioavailability, less environmental impact, removal of toxins in feed.	Through carry-over from consumption of animal products (such as meat, milk). Animal welfare may also be an issue.	Theoretically, any nanosized mineral, vitamin, or other additives and supplements developed for food and health food applications can equally be used for animal feed. .	Some examples of nanosized additives that have specifically been developed (or are under development) for animal feed are available. A number of developments are understood to be at R&D stage. These include nanomaterials that can bind and remove toxins (e.g. mycotoxins), or pathogens in animal feed.

Title: General Insights on Issues Emerging from Food Applications
Name: Qasim Chaudhry[11] and Laurence Castle[11]

1.0   Introduction

Rapid advancements in nanosciences and nanotechnologies in recent years have opened up new prospects for so many industrial and consumer sectors that they have been regarded as the hotbed of a new industrial revolution. The food sector, which itself is worth around 4 trillion US$ per annum globally, is an obvious and prime target of these new developments. The current level of applications in food and related sectors is, however, new emergent. The initial focus of nanotechnology applications has been on food packaging and health-food products, with only a few applications so far in the mainstream food and beverage areas. Although the number of available products has steadily increased worldwide over recent years, most applications are still at R&D or near-market stages. The information relating to the current scale of commercial activity in this field is also very patchy. Because of this, estimates of the current and future market size of nanotechnology-enabled food products vary widely. In 2006, the global market value for nano-enabled food and food packaging products was estimated at around US$4 million, predicted to range between US$6 billion by 2012[12] and >US$20 billion by 2010[13]. According to the estimates, food packaging applications form the largest share of the current and short-term predicted market for nano-enabled products in the food sector. The most promising growth areas identified for the near-future include 'Active' and 'Smart' packaging, health-foods, and functional food products. Reports have also suggested that the number of companies undertaking R&D in food related applications could be between 200 to 400**Error! Bookmark not defined.**[14], including some major international food and beverage companies. It is widely expected that there will be many more new developments in the coming years, and that it could have a major impact on the whole of agricultural and food sectors.

Market reports suggest that the nanofood sector is currently led by the USA, followed by Japan and China, whereas Asian countries (led by China) have been predicted to be the biggest future market for nanofood products**Error! Bookmark not defined.**. Considering the fact that rapid advancements in nanotechnologies have also raised a number of technological, health and safety, regulatory and societal issues, it is likely that the developing countries will lag behind the developed world in terms of technical knowledge and expertise, production/processing capacity, quality control, safety assessment, regulatory controls etc. It is also possible that because of less well developed regulatory and other control systems, developing countries will offer a more open market for nano-food products in the future.

2.0   Current state of developments

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[11] The Food and Environment Research Agency, Sand Hutton, York, Y041 1LZ United Kingdom qasim.chaudhry@fera.gsi.gov.uk.
[12] Cientifica Report. 2006. "Nanotechnologies in the Food Industry" published August 2006. www.cientifica.com/www/details.php?id=47.
[13] Helmut Kaiser Consultancy, Study: nanotechnology in food and food processing industry worldwide 2003–2006–2010–2015, 2004, available at www.hkc22.com/Nanofood.html.
[14] Institute of Food Science and Technology (IFST) Trust Fund. 2006. Nanotechnology information statement www.ifst.org/uploadedfiles/cms/store/attachments/nanotechnology.pdf.

2.1 Applications for food production

The main applications of nanotechnologies for food production include the potential use of nano formulated agrochemicals (e.g. fertilizers, pesticides, veterinary medicines) for improved efficacy, less use of farm chemicals, better control of applications (e.g. slow release pesticides), safer animal feeds (e.g. fortified with nano-supplements, antimicrobial additives; detoxifying nanomaterials), and nano-biosensors for animal disease diagnostics. Example applications include nano-sized feed supplements (vitamins, minerals), feed additive such as a biopolymer derived from yeast cell wall that can bind mycotoxins to protect animals against mycotoxicosis, and an aflatoxin-binding nano-additive for animal feed derived from modified nanoclay[15]. Another example is polystyrene nanoparticle with polyethylene glycol linker and mannose targeting biomolecule that can potentially bind and remove food-borne pathogens in animal feed.[16] Nano-encapsulated and solid lipid nanoparticles have also been explored for the delivery of agrochemicals.[17] However, despite a great deal of interest in the possible use of nanotechnologies in food production area, examples of the available products at present are still very scarce, and most developments in this area seem to be currently at R&D stage. Such applications, nevertheless, have the potential for adoption at a very large-scale by the agricultural sector worldwide. In view of this, it is important to develop adequate risk management strategies, because some of the applications (e.g. nano-pesticides) may pose a risk to farm workers, the environment, and the consumers through potential carryover of residues in food products.

2.2 Applications for Food Processing

The main applications for the food processing area include the use of nano food ingredients/additives in the form of:

- processed food nanostructures for improved or new tastes, textures, mouth-feels. Nano-structuring of natural food materials can potentially enable the use of less fat but still better tasting food products. A typical product in this technology would be a nano-structured ice cream, mayonnaise or spread, which is low-fat but as "creamy" in texture as the full-fat equivalent. Such products would therefore offer a 'healthy' option to the consumer.

- nano-sized or nano-encapsulated food additives and supplements for improved dispersibility of fat-soluble additives in food products, improved or new food tastes, hygienic food storage, reduced use of fat, salt, sugar and preservatives; enhanced uptake and bioavailability of nutrients and supplements. Currently available examples include vitamins, antioxidants, colours, flavours, and preservatives. Also developed for use in food products are nano-sized carrier systems for nutrients and supplements. These are based on nanoencapsulated substances in liposomes, micelles or protein based carriers. The nano-carrier systems are also used for taste masking of certain ingredients and additives, or to protect them from degradation during processing. Examples include food additives, such as a synthetic form of the tomato carotenoid

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[15] YingHua, S., ZiRong, X., JianLei, F., CaiHong, H., MeiSheng, X. (2005) In vitro adsorption of aflatoxin adsorbing nano-additive for aflatoxin B1, B2, G1, G2, Scientia Agricultura Sinica, 38 (5) 1069-1072.

[16] Kuzma, J., Romanchek, J. & Kokotovich, A. 2008. Upstream oversight assessment for agrifood nanotechnology. Risk Anal., 28: 1081–1098

[17] Frederiksen, H. K., Kristensen, H. G. and Pedersen, M. (2003) Solid lipid microparticle formulations of the pyrethroid gamma-cyhalothrin-incompatibility of the lipid and the pyrethroid and biological properties of the formulations. J Control Release 86 (2-3): 243-52.

(lycopene), benzoic acid, citric acid, ascorbic acid, and supplements such as vitamins A and E, isoflavones, ß-carotene, lutein, omega-3 fatty acids, coenzyme-Q10.

- A few inorganic nanomaterials may potentially be used in (health)food products. These include transition metals (e.g. silver, iron, titanium dioxide); alkaline earth metals (e.g. calcium, magnesium); and non metals (e.g. selenium, silicates). Food packaging is currently the major area of application of metal and metal-oxide nanomaterials. Examples include plastic-polymer composites with nano-clay for gas barrier, nano-silver and nano-zinc oxide for antimicrobial action, nano-titanium dioxide for UV protection, nano-titanium nitride for mechanical strength and as a processing aid, nano-silica for hydrophobic surface coating etc. The use of nano-silver as an antimicrobial, antiodorant, and a (proclaimed) health supplement has already surpassed all other nanomaterials used in different sectors.[18] The current use of nano-silver is mainly for health-food and packaging applications, but its use as an additive in antibacterial wheat flour is the subject of a recent patent application.[19] Nano-silica is reported to be used in food contact surfaces and food packaging applications, and some reports suggest its use in clearing of beers and wines, and as a free flowing agent in powdered soups. The conventional bulk forms of silica and titanium dioxide are permitted food additives (SiO_2, E551, and TiO_2, E171), but there is a concern that the conventional forms may also contain a nano-sized fraction due to natural size range variation.[20] A patent (US Patent US5741505) describes nano-scale inorganic coatings applied directly on food surface to provide moisture or oxygen barrier and thus improve shelf life and/or the flavour impact of foods. The materials used for the nano-coatings, applied in a continuous process as a thin amorphous film of 50 nm or less, include titanium dioxide. Another example is that of nano-selenium, which is being marketed as an additive to a tea product in China for a number of (proclaimed) health benefits.
- Surface functionalized nanomaterials are being developed that may add a certain functionality to food or packaging products. Current examples include the use of organically-modified nanoclays in food packaging applications. However, due to the possible convergence of nanotechnologies with other technologies (e.g. biotechnology), the development of new functionalized nanomaterials is likely to grow in the future.

2.3   Applications for Food Packaging

Whilst most nanotechnology applications for food and beverages are currently at R&D or near-market stages, applications for food packaging are rapidly becoming a commercial reality.[21] Food packaging applications form the largest share of the current and short-term

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[18] Woodrow Wilson International Centre for Scholars (2008) The Nanotechnology Consumer Inventory Available at: www.nanotechproject.org/inventories/consumer/, accessed 16 September 2008.

[19] Park K.H. (South Korea) Preparation method antibacterial wheat flour by using silver nanoparticles, Korean Intellectual Property Office (KIPO) Publication number/date 1020050101529A/24.10.2005.

[20] EFSA - European Food Safety Authority (2009) Scientific Opinion on 'The Potential Risks Arising from Nanoscience and Nanotechnologies on Food and Feed Safety', Scientific Opinion of the Scientific Committee, adopted on 10 February 2009, The EFSA Journal (2009) 958, 1-39.

[21] Chaudhry, Q., Castle, L. and Watkins, R. (Editors) (2010) Nanotechnologies in Food, Royal Society of Chemistry Publishers (ISBN 978-0-85404-169-5).

predicted market for nano-enabled products in the food sector.**Error! Bookmark not defined.** It has been estimated that nanotechnology-derived packaging (including food packaging) will make up to 19% of the share of nanotechnology-enabled products and applications in the global consumer goods industry by 2015.[22] The main applications of nanotechnologies for food packaging include the development of nanomaterial-polymer composites for:

- Improved packaging properties (flexibility, durability, temperature/moisture stability, gas-barrier properties)
- 'Active' packaging: polymers incorporating nanomaterials with antimicrobial properties
- Nano-coatings to develop hygienic food contact surfaces and materials, and hydrophobic coatings for self-cleaning surfaces
- Nano-(bio)sensors for 'Smart' packaging concepts

Examples include plastic polymers with nano-clay as gas barrier, nano-silver and nano-zinc oxide for antimicrobial action, nano-titanium dioxide for UV protection, nano-titanium nitride for mechanical strength and as a processing aid, nano-silica for surface coating etc.

2.4   Other applications
Other applications of nanotechnologies that might impact on food safety and quality include the use of nano-porous materials for water filtration and for removal of undesirable tastes, flavours or allergens; certain nanomaterials (e.g. zero valent iron) for water decontamination, nano-coatings (e.g. of titanium dioxide) for photocatalytic sterilization of surfaces and water, nano(bio)sensors for food safety; and nano-barcodes for food authenticity.

3.0   Main projected benefits
The main projected benefits of nanotechnology applications for the food sector include
- More efficient food production methods – less use of agrochemicals (e.g. pesticides, antibiotics; less harm to the environment; less carryover of harmful chemicals residues in food);
- More hygienic food processing (better food safety and quality);
- Novel food products with improved tastes, flavours, mouth feels (healthy/nutritious/tasteful food products);
- Food products with less (or no) preservatives;
- Longer shelf-life of food products (less food waste);
- Innovative lightweight, stronger, functional packaging;
- 'Smart' labels to ensure food authenticity, safety, and traceability.

3.1   Potential risks of nanotechnology applications for the food sector
Currently there are major knowledge gaps in our understanding of the properties, behaviour and effects of the nanomaterials that are (or may be) used for food applications. These knowledge gaps make it difficult to assess the risk of such applications to a consumer, although a careful consideration of the nature of materials and applications can provide a basis for a conceptual risk categorization. For example, products containing natural food nano-structures that are likely to be digested/degraded may not require as detailed an evaluation as the products containing insoluble and potentially biopersistent nanomaterials. On the basis of this, the following broad application categories may be considered:

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[22] Nanoposts report, Nanotechnology and Consumer Goods – Market and Applications to 2015, 2008, published by Nanoposts.com.

- Areas of least concern: Processed (natural) nano-structures in food, that are solubilized or digested in the gastrointestinal tract, and are non-biopersistent.
- Areas of some concern: Nano-carrier systems for food/feed additives that may not be biopersistent but may carry the encapsulated substances across the GI tract. The tissue distribution of the materials contained in such nano-carriers may be different from that of conventional equivalents. An increased bioavailability of some additives (e.g. some preservatives) may lead to increased health risk.
- Areas of major concern: The use of insoluble, indigestible, and potentially biopersistent nano additives (e.g. some metals/oxides), and the potential use of functionalized nanomaterials in food products. These applications may pose a potential exposure to insoluble biopersistent nanoparticles, or functional nanomaterials – the ADME and toxicological properties of which may not fully known at present. Some of the projected applications in the agricultural sector (e.g. nano-pesticides) will also fall in this category.

It is of note that acutely toxic materials are not likely to be used knowingly in food products. The main concerns over consumer safety therefore relate to long term/new or unforeseen harmful effects of exposure to nanomaterials. Nano-additives in food are also likely to undergo a number of transformations in food and the gastrointestinal system due to agglomeration, aggregation, binding with other food components, and reaction with stomach acid, enzymes, and other biotransformation in the body. Such transformation are likely to change the uptake and bioavailability of the materials in the body. However, there is currently little understanding of the impact of such transformation on the safety of nano-food products.

Any potential risk arising from nanotechnology-derived food contact materials will be dependent on the migration behaviour of nanomaterials from packaging. The few experimental and modelling studies carried out so far[23,24,25] suggest the likelihood of nanomaterial migration from polymer packaging to be either nil or very low. On the basis of modelling,[26] it can be predicted that any detectable migration of nanoparticles from packaging to food can only take place where very small nanoparticles (in the lower nm range) have been incorporated in a polymer matrix that has a relatively low dynamic viscosity, and the particles are not bound to the polymer matrix. This provides some reassurance in the safety of nanotechnology-derived food contact materials.

4.0 Regulatory aspects

A number of reviews have shown that developments in nanotechnologies are not taking place in a regulatory vacuum, as the potential risks will be controlled under the existing

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[23] Avella, M., De Vlieger, J.J., Errico, M.E., Fischer, S., Vacca, P., and Volpe, M.G. (2005) Biodegradable starch/clay nanocomposite films for food packaging applications. Food Chemistry. 93: 467-474.

[24] Bradley, E.L., Castle, L. and Chaudhry, Q. Nanoparticles in food contact materials and articles, 2010, in preparation.

[25] EFSA (2008) 21st list of substances for food contact materials, Scientific Opinion of the Panel on food contact materials, enzymes, flavourings and processing aids (CEF) (Question No EFSA-Q-2005-151, EFSA-Q-2006-324, EFSA-Q-2006-323), Adopted on 27 November 2008, The EFSA Journal (2008) 888-890, 1-14.

[26] Šimon, P., Chaudhry, Q., and Bakoš, D. (2008) Migration of engineered nanoparticles from polymer packaging to food – a physicochemical view, Journal of Food and Nutrition Research 47(3): 105-113.

frameworks.[27] The current regulatory frameworks for food and food contact materials in different jurisdictions, such as the European Union, the United States, and Australia are broad enough to 'capture' nanotechnology applications in the food sector. These include regulations relating to general food safety, food additives, novel foods, specific health claims, chemical safety, food contact materials, water quality, and other specific regulations on the use of certain chemicals in food production/protection, such as biocides, pesticides, veterinary medicines etc.[28] The environmental regulations are also likely to capture the use of nanotechnologies in food packaging, and agri-food production applications.

5.0   Current major gaps in knowledge

– A clear, fit-for-purpose, definition of nanomaterials and technologies is lacking. It is being considered at the moment under the recast of the food laws in Europe.
– Validated methods for detection and characterization of nanomaterials in complex food matrices are not available. A few research projects are currently underway in this area.
– Toxicological research on nanomaterial safety is in its infancy. Some common themes have, however, started to emerge from research projects that are underway in this area. This knowledge needs to be periodically pooled and reviewed to draw some conclusions.
– ADME profiles of nanomaterials may be different from bulk equivalents, and it is not known how the ingested nanoparticles will behave in the body. Again research in this area is at early stages.
– The long term health consequences (if any) of ingestion of insoluble and biopersistent nanoparticles via food are unknown.
– There is little understanding of the potential emergence of functional nano(bio)materials through the convergence of nanotechnologies and biotechnologies.
– Guidance on risk assessment methodologies is patchy. In Europe, an EFSA Working Group is currently working on this.
– There are some uncertainties over regulatory control of nanotechnology-enabled food products. For example, over clearly defined responsibility/liability for relevant products and applications, appropriate permissible limits that relate to the (potential) effects of nano-substances in food, and an exclusive premarket approval system for nano-enabled food products. There are some regulatory developments currently in the pipeline – e.g. the recast of the key European regulatory instruments, such as Regulation 258/97 (the Novel Foods Regulation), which is expected to include a specific reference to foods modified by new production processes 'such as nanotechnology and nanoscience, which may have an impact on food'.

6.0   Options for addressing the challenges

– Establishment of international research networks that can address different aspects of the existing and new nanotechnology applications in agriculture and food sectors – i.e. not only the benefits but also the potential risks to the consumer and the environment.
– Development of clear and consistent guidelines for risk assessment of nano-food products.

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- Establishment of a global body that can ensure quality control (i.e. a product indeed has been derived from nanotechnologies and not just labelled for a commercial gain – or vice versa), and safety of nano-food products.
- Promotion of industry best practices and self-regulation in the use of nanotechnologies for food and related applications.
- Appropriate regulatory system at the global level that ensures pre-market evaluation of nano-food products, sets liabilities, and sets clear limits for any nano-additives in food and related applications.
- Possible labelling of nano-food products to inform the consumer.

7.0   Conclusion

An overview of nanotechnology applications in the food and related sectors shows that they offer a variety of benefits to the whole of food chain – from new and improved tastes, textures, to a potential reduction in the dietary intake of fat and other food additives, improved absorption of nutrients and supplements, preservation of quality and freshness, and better traceability and security of food products. The current level of application in the food sector is, however, only small and most products and applications are still at R&D stage. The possible use of some insoluble and potentially biopersistent nanomaterials in food products has also raised concerns over their safety to consumer health and the environment. At present, there are a number of major knowledge gaps in regard to our understanding of the properties, behaviour and effects of nanomaterials. The existence of stringent regulatory controls in many countries provides some reassurance that only safe products and applications of nanotechnologies will be permitted on the market. However, there is a need for a pragmatic approach to a case-by-case pre-market safety evaluation of the nanotechnology-derived food products.

Title: Nanosized and nanomaterial based (bio)sensors- Nano2Biosensors
Name: Arben Merkoçi[29]

Introduction

Detection and identification of pathogenic microorganisms and toxins in foods are the essential steps to take in order to initiate the process of Risk Analysis for the mitigation of food safety risks. Biosensors, originated from the integration of molecular biology and information technology, could provide inspectors, food processing operators and food safety authorities with the ability to rapidly detect pathogens and potential contaminates, including chemical/biological agents. Enhanced screening and surveillance of food sources will significantly improve food safety, thereby reducing the health risks and medical costs associated with foodborne illness.

Despite the recent advances in food pathogen detection, many challenges and opportunities to improve the current technology in order to have simple, rapid, versatile, and inexpensive tools for detection of food contaminants still exist. In theses recent years, the advent of nanotechnology applications in Food safety (i.e. detection systems, biosensors etc) is becoming a key focus of research and development, and the potential benefits of this emerging technology are receiving growing attention from both the public and the private sector. In this context of special interest are the 'nanosized' and nanomaterial   (macrosized) based biosensors - Nano2Biosensors – a modern and efficient class of detection systems. The application of Nano2Biosensors in food industry could lead to immense improvements in quality control, food safety, and traceability. The advantages of Nano2Biosensors can lead to their use in various food industry processes: from raw material preparation, food processing (quality control), monitoring of storage conditions etc. These devices both act as cost effective tools for quality & process controls and ensure food safety.

Advantages of Nano2Biosensors

A large range of biosensors are already available for laboratory use. Several 'Nanosized' and nanomaterial (macrosized) based biosensors – called here Nano2Biosensors- based on optical and electrical techniques are being developed. These are based on nanoscience and nanotechnology related concepts and materials. Nano2Biosensors have a great potential for application in food analysis, in both quality and safety control. Nano2Biosensors can be used to detect several compounds: DNA, protein, cells or pollutants such as heavy metals, pesticides etc. Some interesting Nano2Biosensors based on the use of nanoparticles and techniques such as optical microscopy (i.e. based in light absorption, scattering, fluorescence of nanoparticles) and electrochemistry (i.e. stripping analysis, potentiometry etc.) have been developed and reported in several journal publications (even by our group) and patents.

Nano2Biosensors can achieve very low detection limits (even single molecule or cell). In addition, they offer multidetection possibilities and may ensure high stability (i.e. nanoparticles such as quantum dots are more stable than enzymes or fluorescence dyes). The main advantage (beside the reduction of reagent volumes, detection time, keeping the same sensitivity) is their user-friendly applicability: there is no need for professional users. The idea

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is to develop one-push button-like devices that can give a fast 'yes-no' response or ensure a similar simple communication with the end-user.

Due to miniaturization and mass production possibilities (micro & nanofabrication, nanomaterial synthesis etc.) lower cost Nano2Biosensors can be fabricated ensuring the required efficiency for applications in the food field. The assumptions that need to be met for this direction of development seem to be related to investment and market. Strong cooperation between research groups /institutes and companies is necessary.

Costs and technical capacity/knowledge needed to apply the technology

Nano2Biosensors technologies fit very well into user-friendly and in-field application devices (including implanted devices that can be used to monitor inside food/bioprocess reactors and even, theoretically, inside living organisms, plants for basic studies). These biosensors can be applied in different ways. The type of application would depend on the food area, analyte to be detected, frequency of measurements as well as other factors that as a whole would affect the cost. If a mass production of these devices were achieved, cost issues would be overcome and consequently, the accessibility to this technology and its products in general wouldn't be an important issue, especially for developing countries.

Scientific and technological barriers /obstacles

Several scientific and technological barriers and obstacles must be overcome before the Nano2Biosensors' benefits can be effectively used in contaminants detection in real food systems. The developed Nano2Biosensor are shown to be excellent tools for laboratory applications, but due to reproducibility problems, as well as interferences, their application in real samples is still limited. The identification of major disadvantages would depend on the application. For example the detection of DNA using simple biosensors cannot be compared in terms of sensitivity by standard /laboratory conventional/methods that use, for example, PCR.

Environmental and human health risks need to be carefully considered. Usually, as with all the other assays that involve a variety of chemicals/reagents, safety issues need to be considered. There is a lot of concern related to the toxicity of these materials (i.e. nanoparticles, nanowires, carbon nanotubes etc.), especially for biosensors based on nanomaterials. The evaluation of these effects is still in process. A careful study is required for in-vivo uses in order to achieve the correct conclusions.

Strategies to overcome the challenges

To overcome the challenges of Nano2Biosensor technology and its applications in food field a more detailed study related to interferences for real sample analysis as well as technological aspects related to final application (the interested analyte to be detected) need to be addressed.

Point strategies to overcome the challenges should be:

In-field applications. Substantial effort needs to be made so as to overcome problems related to applications in real samples. Avoidance of interferences coming from sample matrix is the key point for success.

Detection limits. Reaching of low detection limits (detection of few molecules, cells) in a relatively high volume of samples (i.e. 1 molecule or 1 cell in 1mL food sample) requires the development of fast and efficient preconcentration tools/routes based on nano & microfabrication.

Market opportunities. The entrance of Nano2Biosensors in the food market needs to overcome the general cost/efficiency/applicability parameters. Industries and other agency investments in Nano2Biosensor is crucial.

The expected timelines for development

The timelines for development would depend on the kind of application made, as well as the funding of the research/application/technological development projects. This may take from one to several years. For example, sensors for mycotoxins (i.e. aflatoxin) are currently being developed. These are based on various biosensing transduction modes (i.e. electrochemical such as amperometric etc. or optical such as surface plasmon resonance etc.) and assays principles (immunoassays, enzymatic inhibition etc.). Nevertheless, areas where there does not seem to be a lot of promise for the Nano2Biosensors technology are in in-situ applications (i.e. implanted sensors), which seem still to be difficult due to stability issues. The most important difficulties are related to the stability of biological materials used as receptors (i.e. enzymes, antibodies, cells).

Conclusions

We are currently addressing some of the challenges related to Nano2Biosensor technology and its application in food related fields. For sensors related to *in-field* applications (bringing the sample to the sensor, or inserting sensor inside the sample during a determined period of time) we are almost on schedule, but for *in-situ* ones(implanted sensor for long term /automatic monitoring inside the process /plants) there is still a relatively long way to go.

Some of the Nano2Biosensors technologies (i.e. electrochemical sensors, lateral flow) require neither a lot of investment, nor high tech instrumentation for research. Developing countries are, in fact, involved in this kind of research & applications which would make them very good candidates for a fast approach of these technologies.

The application of these sensing systems would have a global effect making a special impact on developing countries. This would be related to the security of food and food processing not only for the security of local people, but also for others, such as visitors to these countries or food importers from these countries. The quality indicators tested *in-situ* through biosensing systems would be added value of the food products being exported to other places in the world. This would also highly benefit the developing countries due to a faster and more efficient processing of food products.

Title: Application of Nanotechnology in Food Safety Assessment: Nano-Tracking Systems – Nanosensors.

Name: Ibtisam E. Tothill[30]

Introduction

Current and future concerns related to food safety and quality requires a multidisciplinary approach based on new generation of innovative technologies such as sensors/biosensors and tools to be used along the food chain. Applications include food pathogens and spoilage microorganisms, food contaminants such as toxins, pharmaceuticals, pesticides, heavy metals etc. The need for products control at different critical steps of the food chain such as of raw materials and food supply, improvement of food processing, monitoring of storage and logistics, and control of safety and quality of final products are essential to ensure food safety. Environmental pollutants and their impact on human's health have also increased the demands for monitoring the air, water and soil for contaminants that might impact on food safety. This needs a multidisciplinary know-how and the use of advanced technology for developing systems with clear innovative solutions to specific safety, quality and analytical requirements. The use of an integrated intelligence approach which will allow full interconnection and communication of multisensing systems is also advantages for food tractability. The use of nanotechnology inspired systems will be powerful in delivering and fulfilling these requirements.

Biosensors and affinity sensor devices have the ability to provide rapid, cost effective, specific and reliable quantitative and qualitative analysis in the food sector (Tothill 2001, 2003; Tothill & Turner, 2003). The increase in the number of analytes requiring monitoring and control with the increase in pressure to comply with legislations have stimulated considerable interest in developing multiarray sensors based on micro and nano systems as diagnostics and risk assessment tools. To date the technology is moving at a rapid pace with developments in novel biorecognition nanomaterials which can be used as the sensing receptors and advances in transducer technology at the nanoscale has resulted in more emerging products for multiplex analysis and nano-tracking systems which are feasible to fulfil the rapid monitoring and control need of the food chain. Micro and nano systems developed for logistic food surveillance by means of implementation of multisensing systems is also revolutionizing food tracking. New advances in lab-on-a- chip technology, microarray and nanotechnology are also having a high impact on developing biosensors with new capabilities.

Advantages in the use of nanotechnology for food safety

Food producers are under pressure from crop disease and environmental conditions which threaten their profit margins. Also quality assurance along the food chain has made food safety and tractability a priority. Therefore, the use of lab-on -a-chip approach for the analysis of disease markers/contaminants at the same time will be cost effective and highly beneficial for the food industry in ensuring the safety and quality of the food and also for risk

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assessment and management. Nanotechnology has the potential to improve food quality and safety significantly through the use of advanced sensors and tracking systems.

The use of nanomaterials and structures such as semiconductors and conducting polymer nanowires, carbon nanotubes, silica nanoparticles and labels for biosensor applications is expanding rapidly and to date many comprehensive review articles have been published in this area (Katz and Willner 2004, Katz et al., 2004; Willner et al., 2007; Kerman et al., 2008). The application of nanotechnology in biosensors can range from the transducer device, the recognition ligand, the label and the running systems. Their application in sensor development has been due to the excellent advantages offered by these materials in miniturization of the devices, signal enhancements and amplification of signal by the use of nanoparticles as labels. These can increase sensitivity of the final devices and also allow the fabrication of multiplex sensor systems such as high density protein arrays (Jain, 2004). The high surface to volume ratio offered by nanomaterials makes these devices very sensitive and can allow a single molecule detection which is very attractive in contaminant monitoring such as toxins. The use of nanowire transducers can also offer greater sensitivity in affinity sensors (Woolley et al., 2000; Wang et al., 2005).

The use of luminescent nanocrystals (Quantum dots) as molecular labels to replace fluorophores has created new applications for nanomaterials in labeling and visualization. These nanocrystals can be attached as labels for antibodies and other molecules to detect different analytes at the same time (multiplex sensing). Quantum dots show distinct advantages over other markers due to their spectroscopic properties and narrow emission peaks and therefore their use in multiplexed analysis is increasing. Their high emission quantum yield result in improved signal /noise ratio and therefore decrease false readings (negative and positive).

The use of striping voltammetry for detecting metal nanoparticles has been applied where these metals has been used as marker tags. Gold and silver nanoparticles can be used in these methods including different inorganic nanocrystals (e.g. ZnS, PbS, CdS) for analytes detection. The unique physical and chemical properties of nanoparticles such as colloidal gold can provide excellent application in a wide range of biosensing techniques (Rosi and Mirkin, 2005). Several products are available on the market such as Oxanica (UK) Quantum dots and MultiPlxBeads™ from Crystalplex Corp., USA. Nanoparticles can also be exploited in conductivity based sensors where they can induce a change in the signal upon the attachment of the nanoparticles- antibody tagged with the captured antigen on the sensor surface. Gold nanoparticles are easy to functionalize and are used for antibody immobilization, making this process more reducible.

The development of micro/nanosensor devices for toxins analysis is increasing due to their extremely attractive characteristics for this application. Their novel electron transport properties make them highly sensitive for low levels detection (Wang, 2005, Logrieco et al., 2005). The multiplex analysis capability is also very attractive for multi biomarker analysis. The development of methods of near real time pathogen and disease detection and location using micro (MEMS) and nano multisensory systems with new chip designs and capabilities will allow analysis to be taking place before the product reach the consumer. Multi toxins detection (e.g Mycotoxins) in foods can be conducted using single miro/nanoelectrode array chip with high sensitivity and rapid analysis time. Therefore, the application of lab-on-a-chip using semiconductor fabrication techniques is expanding in all areas of analysis due to the advantages of using small samples to analyse several microorganisms/toxins i.e offer high

throughput analysis. Productivity would increase through diagnosing disease early, so that action can be taken early to control the problem. The use of micro/nanoarrays for analysis applications in foods can produce highly sensitive sensors.

At Cranfield we are developing novel nanomatrials and also using commercially available nanoparticles such as gold and silica and micor/nano arrays as transducers for toxins, bacteria and other biomarkers analysis to enhance the signal achieved on the surface of the electrochemical sensor, QCM and SPR sensor systems and also for multiplex analysis for several biomarkers (Tothill et al., 2001; Tothill, 2009; Parker et al., 2009; Tothill, 2010; Uludag & Tothill, 2010)

New legislations introduced both in the EU and the USA indicate that tracing food from the field to the factory and then to the supermarket shelf is a legal obligation. The use of radio frequency identification (RFID) technology has been implemented by retailers to track the food and automat its traceability. New developments in nanomaterials and nanosensors/nanosystems have the ability of produce new and advanced traceability tools. Nanoscale Identity Preservation (IP) is a technique that could lead to the continuous tracking and recording of agricultural batches and the conditions they are being exposed to. Sensors could then be linked to recording and tracking devices using wireless and blue tooth technology. Nanosensors embedded in food packages can then be used as electronic barcodes which allow traceability and tracking combined with food spoilage markers and deterioration monitoring, increasing the capability of current technologies.

Challenges facing technology development

The application of nanotechnology in the development of nanodevices for sensing and tracking face many challenges. The technology is still developing and therefore many issues and problems still need to be resolved regarding producing viable systems suitable as commercial products. Also the variety of biological complexity of molecular structures and the wide range of concentrations need to be detected, coupled with the complexity of the food matrices are some of the bio-analytical challenges facing the application of nanodevices for food analysis. The stability of some nanomaterials such as quantum dots needs improving, reduce aggregation in use conditions and also reduce cost as they are expensive to date. Problems associated with sample treatment, delivery to the nanosensor devices still require extensive investigation to develop a better microfludic systems and informatics tools for signal output.

Currently a lot of work is being carried out with huge investments from industry and governments to develop nanosensors and nanosystems targeting improved detection (sensitivity and selectivity), multiplexing analysis (analysing several analytes at the same time), rapid out (short analysis time), on-site in field analysis (portable devices), and cost effective (low cost compared to lab based analysis). These are big challenges which will require few years of research and developments before they can be materialized.

Key concerns regarding technology implimentation

Concerns about the use of nanotechnology in this particular application is limited due to low exposure of food to the toxicity risks associated with nanomaterials, since food samples are usually disposed of after analysis. Therefore the risk is only reduced to the wider issue of toxicity risks for humans and the environment after the disposable of these devices and materials. In nano-tracking, loss of privacy may be of concern as nano surveillance will be

able to track each step in the food chain. This may have impact on the food producer, the manufacturer and also the consumer.

We should however, take the signs associated with the toxicity of nanoparticles very seriously and ensure and control there safe disposal, especially the potential risks posed by engineered nanoparticles, until further studies proof otherwise.

Conclusion

The biosensor field is moving forward at a rapid pace with developments and innovation taking place at all levels including the sensing receptor, the transducer and the accompanying electronics and software. As we progress from single analyte testing to multianalyte analysis, miniaturization and nanotechnology playing a big part in producing highly sensitive and cost effective devices.

There are very attractive technologies being developed for food safety and tractability which can be applied at all levels whether it is in the farm or the factory and can be operated for on - site analysis by unskilled personnel. Trends to further develop and produce chip-based mico/nanoarrays for multi analyte analysis will continue and this will have significant impact on risk assessment testing. The introduction of the diverse array of nanomaterials such as gold and silver nanoparticles and other metal oxides such as quantum dots for diagnostics application will enhance and elevate the capability of the biosensor technology. Also the advances in silicon fabrication technologies is producing more defined and reproducible array devices and that will add further improvement on the final sensing devices. This however, needs to be combined with developments in sampling acquisition and sample handling procedures.

Bio- and affinity sensors have the potential to provide rapid and specific sensing for food quality assurance. Analysing contaminants (chemical and microbiological) at the required legislative limit require highly sensitive devices that allow rapid diagnosis. Also it is advantages for these techniques to be portable since a large number of analyses could benefit from on-site testing for risks assessment and management. Therefore, there is a need for simple and sensitive diagnostics methods that can detect multiple analytes which exist at low concentrations in different foods and feeds matrixes. However, biosensor devices need to be further developed to face these challenges such as multiplex analysis where arrays of sensors need to be developed at the same chip. Innovation in nanotechnology to include analysis software and micro/nanofluidics can aid in the development of such devices. Applying nanomaterials in the development of the sensors will make these devices highly sensitive and more applicable for lab-on-a chip diagnosis. Early and sensitive detection will aid in eliminating contaminants from interring the food chain and preventing ill health and protecting life. Therefore these rapid technologies need to be developed further using appropriate funding to move the technology from research to commercial products.

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Title: Nanotechnology for Bioplastics: Opportunities, Challenges and Strategies
Name: Jose M. LAGARON [31]

Introduction

Over the last decades there has been a significant increase in the amount of plastics being used in various sectors, particularly in food packaging applications. In fact, the largest application for plastics today is packaging, and within the packaging niche, food packaging is the largest plastics demanding application. This is because plastics bring in enormous advantages, such as thermoweldability, flexibility in thermal and mechanical properties, lightness and low price. However, polymers do also have a number of limitations for certain applications when compared to more traditional materials, like metals and alloys or ceramics. The chief limitation is their impermeability to the transport of low molecular weight components, which leads to issues such as (i) food oxidation by penetration of oxygen, (ii) migration of toxic elements from the plastic and (iii) scalping of food components on the packaging with the consequent losses in food quality attributes. In spite of that, plastic materials continue to expand and replace the conventional use of paperboard, tinplate cans and glass, which have been typically used as monolayer systems in food applications. Initially, most plastic packaging was made of monolayer rigid or flexible materials, but as the advantages of plastic packaging became more established and developed, the increasingly demanding product requirements found when plastics had to suit more and more food products led, (in conjunction with significant advances in plastic processing technologies) to more and more complex polymeric packaging formulations. This resulted in complex multicomponent structures, such as the so-called multilayer packaging based systems widely used today, which in many cases make use of metalized layers. Still, there are significant advantages in terms of costs and other issues such as easy of recycling in developing simpler, less environmentally concerned packaging formulations. As a result, strong efforts in material developments and in material blends have been carried out over the last decades to reduce complexity in food packaging structures and to develop new materials.

On another line, the substantial increase in the use of plastics has also raised a number of environmental concerns from a waste management point of view. As a result, there has been strong research interest, pushed by authorities at national and international levels, and a concomitant industrial growing activity in the development and use of biodegradable and/or biobased materials. On the one hand, "biodegradable" materials can disintegrate and biodegrade through processes such as composting into mostly carbon dioxide and water, hence reducing plastic waste, whereas "biobased" sustainable materials, on the other hand, additionally consume carbon dioxide during their production, hence creating the potential for the new concept of "carbon neutral materials" [1-3].

Amongst biobased materials, three families are usually considered: Polymers directly extracted from biomass, such as the polysaccharides chitosan, starch, carrageenan and

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cellulose; proteins such as gluten, soy and zein; and various lipids. A second family makes use of biomass-derived monomers but uses classical chemical synthetic routes to obtain the final biodegradable and/or renewable polymers, including thermoplastics and thermosets. In regard to thermoplastics, this is the case of polylactic acid (PLA) and the non-biodegradable sugar cane ethanol-derived biopolyethylene [1-3]. The third family makes use of polymers produced by natural or genetically modified micro-organisms such as polyhydroxyalcanoates (PHA) and polypeptides [4]. Amongst non-biobased materials, i.e. using either petroleum-based monomers or mixtures of biobased- and petroleum-based monomers, there are also a number of biodegradable resins such as polycaprolactones (PCL), polyvinyl-alcohol (PVOH) and its copolymers with ethylene (EVOH) and some biopolyesters. Nevertheless, it seems clear that although biodegradability can help reduce plastic waste, from a "green house" perspective, biobased sustainable materials, the so-called bioplastics, are currently considered the way to go and may be the only alternative in the future as fossil resources become exhausted.

Moreover, in order to reduce both energy consumption during the production of bioplastics and to provide additional raw material sources, the valorization of food by-products is the current trend. Food processing effluents or solid wastes are only partially valorized and are mostly disposed in landfill sites where, since they are amenable to putrefaction, they have to be treated according to the restrictions identified by, for instance, the international Landfill Directive. These byproducts are rarely and most recently being used as source of high added values components, such as food ingredients, but they present great potential value for their use in the production of bioplastics.

In spite of the significant potential of bioplastics to substitute petroleum based materials to help reduce environmental concerns, these materials still present a number of property and processing shortages that preclude their use in many applications, particularly in the food packaging field. The reason for this is their generally lower barrier properties to gases and vapours, their strong water sensitivity, lower thermal resistance, shelf-life stability due to aging and a number of processability issues still associated to bioplastics. In this context, nanotechnology brings in significant opportunities to minimize the latter drawbacks.
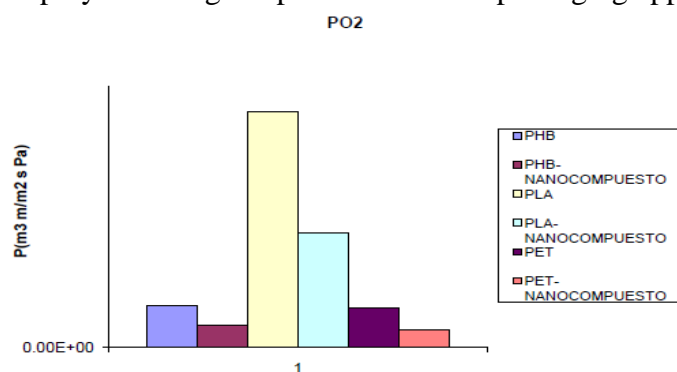
Nanotechnology is by definition the creation and subsequent utilization of structures with at least one dimension in the nanometer length scale that creates novel properties and phenomena otherwise not displayed by either isolated molecules or bulk materials. Since Toyota researchers in the late 1980s found that mechanical, thermal and barrier properties of nylon-nanoclay composite material improved dramatically by reinforcing with less than 5% of nanoclay, extensive research work has been performed in the study of nanocomposites for food packaging applications. The term nanocomposite refers to composite materials containing typically low additions of some kind of nanoparticles, most nanocomposites being considered in the food biopackaging sector are based in low additions, typically 1 to 7 wt.-%, of modified nanoclays [5].

Many nanoscale structures display, at the least, a high surface-to-volume ratio, which becomes ideal for applications that involve composite materials, chemical reactions, drug delivery, controlled and immediate release of substances in active an functional food packaging technologies and energy storage for instance in intelligent food packaging [6,7].

Among the various existing nanotechnologies available, the ones that have attracted more attention in the bioplastics field are the nanoclay-based nanocomposites. It has been broadly

reported in the scientific literature that the addition of low loadings of nanolayered particles, i.e. nanoclays, with thickness in the nanometer scale and with high aspect ratios, to a raw biopolymer can have a profound enhancing effect over some material properties, such as mechanical properties, thermal stability, UV-VIS protection, conductivity, processability and gas and vapour barrier properties [3,5]. Moreover, the addition of nanoadditives does not alter inherently good properties of the matrix to a significant extent, such as transparency and flexibility. Important issues associated to the use of bioplastics, such as the non-intended migration of plastic components to foods, can also be reduced by the use of these nanoclays. Since more recently they also offer great advantages in the formulation of active biopackaging technologies, such as more efficient antioxidant, oxygen scavengings or antimicrobial biopackaging, more direct implications in increasing packaged foods quality and safety have occured.

The graph below shows, as an example, that the performance (in terms of oxygen barriers) of biopolyesters is already significantly improved by melt compounding addition of food contact complying nanoclays. The nanoclay-based PLA, although it approaches the performance of the petroleum-based polyester counterpart polyethylene terephthalate (PET) compared to PLA, does not, as yet, outperform the polyester and further optimization work is required. On the other hand, the nanoclay-based PHB does already outperform PET, hence this microbial biopolymer has good potential in food packaging applications.

Oxygen permeability of PLA, PHB and PET and of their nanocomposites

In terms of costs, the above biopolyesters are already or soon targeted to be, comparable to their petroleum based counterparts as world-wide production capacity continues to grow. Currently, it is estimated that the consumption of petroleum-based plastics amounts to ca. 52 million tons/year, for only ca. 750,000 tons/year for bioplastics. Ideally, the biopolymers cost should be below 2 €/kg for mass replacement of their petroleum based counterparts. Food contact complying nanoclays, on the other hand, are currently mass produced and are said to cost typically below 10 €/kg (provided by NanoBioMatters S.L., Spain) depending on the grade, facts that together with the recommended low dosages, i.e. typically below 5 wt.-%, convert these nanoadditives in truly accessible commodity nanotechs for food biopackaging applications.

Most applications of nanocomposites in bioplastics have made use of laminar clays, but to some extent also of carbon nanotubes and of nanoparticles of metals and oxides. However, there are other types of reinforcing elements, such as biodegradable cellulose nanowhiskers and nanostructures obtained by electrospinning, which are very promising in a number of application fields [8-11]. The use of biobased nanofillers to reinforce bioplastics has the value

of generating fully biobased formulations. These nanobiofillers have a very large surface to mass ratios (up to 10^3 higher than a microfiber), excellent mechanical strength, flexibility, lightness and in some cases edibility since they can be made of food hydrocolloids. The advantage of application of these nanomaterials has already been considered in the control release of bioactive principles in the pharmaceutical and biomedical fields and can also be applied as reinforcing fillers and in the control release of actives and bioactives in food packaging applications and for the nanoencapsulation of functional added-value food additives [12].

Challenges and Strategies

In the bioplastics field the main two challenges are associated to functionality, i.e. generating reproducible petroleum-based performance, and achieving truly positive life-cycle analysis, i.e. achieving the goal of carbon neutral or minimizing energy consumption. In these issues, it is clear that there is "plenty of room at the bottom", despite the great advances made, but there is no doubt that nanotechnology will play a significant role here, since more recently, there is also debate on potential competition between the use of crops for foods and to derive biobased products, in what has been claimed as a cause for recent increases in the price of foods. The latter issue is perhaps not so relevant when it comes to bioplastics, since consumption of food competing resources to make biobased plastics is currently negligible but that can surely be minimized by valorization of food by-products and by optimization of microbial based plastics.

Regarding nanoparticles, it is reckoned that a high nanodispersion should be achieved in the bioplastic matrix to reach the level of performance associated to the use of nanotechs. Hence, nanoparticles dispersion still remains a challenge for the full delivery of the expected properties as announced by the early modelling work. There are several technologies to achieve nanodispersion in bioplastics, the most common being in-situ polymerization, dispersion in solution and dispersion via melt-blending. In spite of the two former being more efficient in achieving nanodispersion in many cases, the latter route, less efficient in achieving dispersion, is without doubt the most demanded technology from an applied view-point, because it makes use of industry available machinery and processes to convert plastics into final articles.

As stated above, most nanocomposite technologies in the market today make use of chemical or otherwise modifications of commodity layered 2:1 or 1:1 phyllosilicates, the so-called nanoclays. Modification is needed to both compatibilize highly hydrophilic clays with the more organic apolar chemical constitution of most thermoplastic polyester biopolymers and to increase the clay intergallery space (basal space between adjacent layers), hence facilitating both intercalation and exfoliation, i.e. nanodispersion, of the clays laminar components in the matrix during compounding. In the food chain, specific caution should be taken because the modifications should be harmless, comply with migration regulations and make use of food contact approved substances as valid surfactants. Currently, many of the existing nanotechs do not comply with the existing legislations.

Thus, it is a very important concern that most of the nanocomposite formulations (first generation nanocomposites) in the market are currently making use of ammonium salts as organophilic chemical modifiers, which have been devised to enhance the properties of engineering polymers in structural applications. However, for food packaging applications as

mentioned above, only food contact approved materials and additives should be used and should do so below their corresponding threshold migration levels. Thus, second generation nanocomposites are, therefore, referred to as nanocomposite formulations, which are specifically designed to comply with current regulations and at the same time are cost effective and specifically formulated to target specific materials (including biopolymers), materials properties or production technologies. In essence, second generation nanocomposites are materials with targeted specifications rather than wide spectrum generic formulations.

Nevertheless and in general, there is a lack of knowledge about the impact of nanomaterials when inserted into bioplastics in applications. For instance, little is known about their stability during processing and potential toxicity issues related to decomposition and/or migration and also how they will affect the current establishment of afterlife disposal channels such as incineration, composting or recycling. However and in regard to this issue, the prospects for natural additives such as food contact complying nanoclays and nanobiofibers may not be of so much concern. For instance, we have found out in our research that nanoclays in biodegradable matrices do not delay biodegradation during composting, since it is a process that occurs from the outside towards the inside and that the nanoclays, due to their inherent high surface energy, re-attach to each other to become microparticles of soil once the polymer matrix disappears. It is also very important regarding inherent nanoparticle hazard assessment to differentiate between three-dimensional nanoparticles (spherical or otherwise 3D nanoparticles such as nanometals), bi-dimensional nanoparticles (nanofibers, with only nanodimensions in the 2D cross-section) and the least concerned, one dimensional nanoparticles (nanoclays with only one nanodimension in the thickness). Thus, nanoclays should be considered aside because in essence they are heat stable microparticles, which remain such all along the process of production, commercialization and, since in commercial products nanodispersion is seldom achieved, also within the biopolymer matrix during service.

Strategies to overcome the above and other pending issues will come from strengthening on the following items:

- The creation of nanotech industry based platforms with solid knowledge of the problems to solve and of the legislation and commercialization barriers ahead should be boosted. Open innovation and development and commercialization of commodity products are a must. Nanotech will only serve to widespread the use of bioplastics by balancing their properties if they become a commodity in terms of pricing and volumes.

- Stronger R&D effort focus to provide real value for nanobiocomposites, i.e. the development of the underpinning science and technology to understand and control the composition/properties/processing/aging relationship of nanobiocomposites.

- Development of new bioplastics and tailor made reinforcing nanobioadditives that make use of only biobased products and resources, particularly derived from valorization of food byproducts.

- Establishment of a clear and knowledge-based legislation worldwide that defines nanoproducts and enables a clear assessment of the liability of existing ones in the various application fields and that provides concise guidelines for the clearance route of new developments. It might be that there is no need to change legislation to accommodate many

existing nanomaterials and, therefore, it is all related to complying with the current global legislation for most of these. But then this has to be clearly stated to industries and society to boost implementation. FDA says 'we regulate products, not technologies', and perhaps this should be the right approach.

- Deepening our understanding regarding the life cycle analysis of nanobiocomposites.

- Deepening our understanding about the potential toxicity of current and under development nanomaterials and of their nanobiocomposites. Characterization of the stability of nanobiocomposites during processing and shelf-life, full migration studies and assessment of issues related to the various disposal channels should be carried out.

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Title: Applications of nanomaterials and nanotechnology in food packaging materials
Name: <u>Laurence Castle</u>, Emma L Bradley and Qasim Chaudhry [32]

Introduction

Nearly all of the food and drink that we buy and then consume is packaged in some way. The main functions of food packaging is to protect and preserve the food, to maintain its quality and safety, and to reduce food waste. There can be no doubt that food packaging materials and technologies have fulfilled these functions. Packaging plays a key role in helping to providing a safe and nutritious food supply. There can be a down-side however and this is the potential for contamination of the food by chemical migration from the packaging. Any chemical migration must be kept under an acceptable level of control. A second consideration is the fate and environmental impact of the packaging when the consumer is finished with it. Packaging materials and packaging technologies have of course developed over the centuries and the possible application of nanomaterials and nanotechnology is one of the most recent steps in this continuing evolution. Other examples include the use of new types of plastics and new formulations of biodegradable materials, and new processing technologies applied to the packaged food such as ionizing radiation, microwave heating and high pressure processing. These materials and processes now exist in the market but as they emerged they were scrutinized for any potentially adverse effect on the safety or the quality of the packaged food. This scrutiny of existing packaging of course continues. In the same way, therefore, potential applications of nanomaterials and nanotechnology in food packaging materials need to be evaluated for safety and then monitored.

This mini-paper focuses on the questions of consumer safety and environmental safety of nanomaterials and nanotechnology used in food packaging materials and the extent to which regulation and market uptake is impeded by current uncertainties. The technical, economic and social aspects of the development, production and commercialization of new food packaging materials is outside the scope here.

Note 1. The term Packaging Materials is used here as convenient shorthand for materials and articles intended to come into contact with foodstuffs. There are other applications of food contact materials (tubing, conveyor belts, cooking utensils etc) but this paper focuses on food packaging materials.

Actual and near-market applications of nanomaterials in food packaging

Whilst most nanotechnology derived food products are still at R&D or near-market stages, applications for food packaging are rapidly becoming a commercial reality. The main developments include:

Improvement of mechanical properties through nanocomposites
Food packaging must protect the food from physical damage and from dirt and insects etc. Food packs must also be easy to handle, be used to dispense the food, and have many other attributes linked to the physical characteristics of the packaging material. The use of nanoparticles (nano in all three dimensions) or nano fibres and rods (nano in two dimensions)

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or nano layers and sheets (nano in one of the three dimensions) can confer useful physical properties to the packaging. Nanomaterials can have unique properties such as strength and stiffness that exceed conventional materials. So unlike some conventional fillers e.g. glass fibres and talc, only a low level of nanomaterials may be sufficient to enhance the performance of the composite materials.
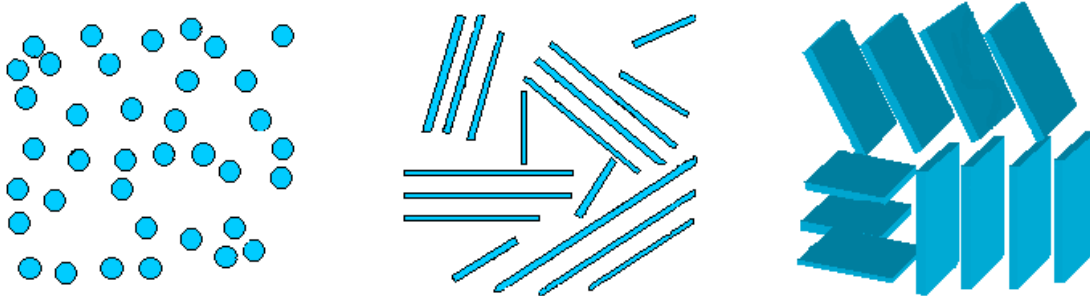

Figure. Nanomaterials as; (a) particles; (b) rods; (c) layers

Improvement of barrier properties
Food packaging must help maintain freshness and protect the food against spoilage by light, oxygen ingress, humidity, taint and odour pick-up or the loss of flavour components. With the increasing moves to light-weighting of materials and to provide extended shelf-life to reduce food waste, materials that are thin but that have high-barrier properties are in great demand. Using nanocomposites (polymer + nanoparticles) or using nano-thin coatings can help provide enhanced barrier performance.

Active packaging

Conventional packaging is intended to be largely "passive" in that it serves a protection and preservation role as a barrier to- and from- the external environment. On the other hand, active packaging concepts exist where the packaging is intended to <u>change</u> the nature or the composition of the food or of the atmosphere that surrounds the food in the pack. Nanomaterials may be used in these active packages. Examples include nanoparticles used for <u>scavenging</u> purposes - removing oxygen or taint & odour chemicals from within the pack. Alternatively, nanoencapsulates may be used to <u>release</u> additives such as preservatives or colours onto the food surface thereby reducing the amount of chemical additive needed.

Surface biocides
These should not be confused with active packaging. For surface biocides, the biocidal agent is intended to help maintain the hygienic condition of the food contact surface by preventing or reducing microbial growth and helping 'cleanability'. There should be no preservative effect on the food. Surface biocides may have a useful function in food processing equipment (e.g. poultry lines) and food handling equipment (e.g. conveyor belts) that are difficult to clean in place. They may also have a role to play in reusable food containers and the inside liners of refrigerators and freezers. Their relevance to single-use disposable packaging is questionable. Since nanomaterials have a very high ratio of surface area to mass, materials such as nano-silver zinc oxide or magnesium oxide may have an effective action as a surface biocide in food contact plastics, rubber, silicones etc.

Note 2. Nanomaterials and nanotechnology may also be used in packaging to confer biodegradability or to confer intelligent functionality. These applications are described in other background documents and they are not discussed here.

Advantages of nanomaterials in food packaging

The main technical benefits offered by nanomaterials and nanotechnology are reflected in the actual or near-market applications above. They include:

Innovation
The main driver for applications of nanomaterials and nanotechnology in food packaging materials is innovation and new product development. New products can give greater consumer choice and convenience. New products can support social change and lifestyles. New products can open new markets and create wealth and employment.

Light-weighting
Using less packaging material but with the same technical performance offers lower material usage. This could give a lower carbon /environmental footprint from the manufacture and transport of the packaging and the packaged food.

Greater protection and preservation of the food
Better barrier properties can help maintain and even increase shelf life without additional chemical preservatives etc. This can provide potentially cheaper food, better nutrition and less food waste.

Costs and capacity needed to access the technology

The main applications described in the literature come from the USA, Japan, several member states of the the EU, Australia, China, Korea, Taiwan and New Zealand, Considering the rapid developments in this field and the global nature of international food companies, it is not unreasonable to anticipate that nanotechnology-derived food packaging could start appearing in many other markets in the next few years.

A distinction can be made between the relatively low resources and know-how necessary to employ nanomaterials in food packaging materials compared to the higher economic and technical requirements to apply nanotechnology in making food packaging materials.

One of the first applications to emerge on the market as improved materials for food packaging were polymer nanocomposites incorporating clay nanoparticles. The nanoclay mineral used in these nanocomposites is montmorillonite (also known as bentonite), which is a natural clay commonly obtained from volcanic ash/rocks. Other polymer nanocomposites incorporate metal (oxide) nanoparticles. These additives can be purchased freely on the open market. They can then be incorporated into polymers and then these polymers ca be converted into packaging materials and articles such as films and containers, all using rather conventional technology. In this respect, aside from the cost of the additives, the economic and technical barriers to entry are low.

On the other hand, for a more significant re-engineering of materials then there are significant cost and technology barriers to entry. Examples include nano-coatings applied in a multi-layer deposition process, either layer-by-layer or by electrostatic self-assembly. Other examples of high technology include hybrid organic-inorganic nanocomposite coatings of hybrid precursors and sol-gel systems. Some coatings are produced using atmospheric plasma technology using dielectric barrier discharges and others such as silica-polymer

hybrids are manufactured by sol-gel processes. These systems are proprietory and the costs of development are not made public.

Key issues to be discussed

There are two key issues of relevance to this discussion paper. The first is food safety and quality and any potential impact on consumers. The question is, would the use of nanomaterials and nanotechnology in food packaging materials, and especially any migration into the food, have any negative impact on the safety or the quality of the food. The second issue is the question of environmental impact - initially on the production of the packaging material but more crucially when it is finished with and disposed of. A specific question pertains to recycling and if using nanomaterials would compromise the performance of existing recycling systems. Regulation and market uptake is impeded by these uncertainties in consumer safety and environmental safety.

Scientific and technical challenges

First, there is a lack of understanding on how to evaluate <u>hazard</u> of nanomaterials by the oral (food) route. This is not a unique knowledge-gap for any migration from food packaging because it applies to all aspects of nanotechnology applications in the food sector. But any possible impact of food packaging on the nature of the hazard has to be considered. - e.g. any effect of polymerization or processing on the size or shape or surface chemistry of nanoparticles has to be evaluated

Second, there is a lack of tools to use to estimate <u>exposure</u>. The central question here is; is there any migration of nanomaterials from packaging into food and, if so, how much.? Depending on how the hazard is characterized (above) information would be needed on the concentration or number of nanoparticles, what type with respect to size, shape and surface chemistry etc. Currently, based on theoretical considerations and the fixed or embedded nature of nanoparticles in food packaging, the expectation is they are not likely to migrate and pose any significant risk to the consumer. But we do not have the analytical measuring tools to confirm this no-migration prediction by actually testing packaged foods.

Third, it may be possible that the high surface area and active surface chemistry of some nanomaterials could give rise to unwanted chemical reactions. So a third problem is if using nanomaterials could <u>potentiate</u> (elevate) the migration of non-nano ingredients or could cause (catalyse) the formation of undesirable reaction products during the processing and fabrication of packaging materials.

Fourth, there is a lack of understanding on the impact of nanomaterials in waste disposal streams. These include re-use, recycling, burning for energy recovery and landfill. The last two are general questions and not specific for nanomaterials in packaging. The specific question on recycling and packaging is, if using nanomaterials e.g. in plastics or glass or paper/board or metal packaging would compromise the performance of existing recycling systems.

Last but not least, the legitimate questions and concerns on nanomaterials have cast a shadow onto some 'conventional' packaging ingredients and processes. These may have a size range that incidentally has a nano fraction or a nano character. Examples include existing fillers,

pigments and surface coatings. This raises the question - what is conventional and what is novel, nano?

Strategies to overcome the challenges

Note 3. Research needs that are generic to nanomaterials such as hazard identification and characterization are not described here. These are described in other background documents. This includes the need to set health-based reference values with which to compare the types and levels of any migration of nanomaterials from food packaging.

Develop the tools to characterize nanomaterials in packaging and to characterize and quantify any migration from packaging into foods. The expectation is that nanomaterials will be fixed or embedded in most types of food packaging and so not be available to migrate. However, tools are needed to examine packaging materials to see if this is correct.

Apply these new tool to test the packaging materials for migration of any man-made nanomaterials. Given the complexity of foods, the testing of packaging for migration often uses food simulants as model foods. These are simple liquids designed to mimic the properties of foods - e.g. aqueous, fatty, alcoholic or acidic. The food simulants have been designed for normal migration of chemicals by diffusion and dissolution. It would need to be checked if they are appropriate for testing for any migration of nanomaterials.

Test existing packaging materials such as plastics, elastomers, coatings and inks etc. to see, if nanomaterials were incorporated into them, could they potentiate migration of chemicals or cause new and unwanted chemicals to be formed and subsequently migrate.

Evaluate existing and foreseeable recycling technologies to see, if nanomaterials were used widely, would they compromise the performance of the recycling streams.

Conclusion

Food packaging applications form the largest share of the current and short-term predicted market for nano-enabled products in the food sector. Regulation and market uptake is impeded by uncertainties in consumer safety and environmental safety. Analytical tools need to be first developed and then applied to test if any nanomaterials and related non-nano associates, migrate from food packaging into food.

Title: Nanotechnology-Enabled Water Treatment and Reuse for Developing Countries: Emerging Opportunities and Challenges

Name: Pedro J.J. Alvarez[33], Qilin Li and Jonathan Brame

Introduction

Ensuring reliable access to inexpensive and clean sources of water is an overriding global challenge noted as one of the Millennium Development Goals of the United Nations. This challenge is rapidly growing as the world's population increases; global climate change threatens to take away a large fraction of already scarce fresh water resource due to seawater intrusion; agriculture and food production draws more and more of the potable water supply; and larger quantities of water are used to produce increasing amounts of energy from traditional sources.

The need for a sustainable and safe water supply is particularly compelling for developing countries not only in rural villages but also in rapidly growing metropolitan areas, due to the faster tendency towards mega-urbanization coupled with a lack of adequate infrastructure to purify water and wastewater. The high energy consumption and risks associated with water quality deterioration during water distribution through aged centralized systems call for both a paradigm shift in water management and for technology reform.

Vision for Distributed Nanotechnology-Enabled Water Treatment and Reuse

Nanotechnology can enable a distributed water reuse and treatment paradigm and offer leapfrogging opportunities to obviate concerns of water quality degradation within distribution networks, alleviate dependence on major system infrastructure, exploit alternative water sources (e.g., recycled "new water") for potable use, and abate energy consumption. Future urban systems will increasingly rely on high-performance nanotechnology-enabled water monitoring, treatment and reuse systems that target a wide variety of water pollutants and are affordable and easy to operate. This will also contribute towards a zero discharge paradigm, which is the ultimate goal of sustainable urban water management. Examples of engineered nanomaterials (ENMs) that can enable this vision are summarized in Table 1. Such novel technologies for water treatment at both point-of-use and community scale are of great value for increasing the robustness of urban water distribution networks, for neighborhoods and buildings that are not connected to a central network, and for emergency response following catastrophic events.

Examples of Research and Development Activities

Although nanotechnology-enabled water treatment and reuse is still far from full-scale application, there is considerable lab scale research activity that has yielded promising results, and several pilot-scale and commercial applications are beginning to emerge (Radjenovic *et al.* 2009, Haldane 2010, He *et al.* 2010). Engineered nanomaterials (ENMs), primarily silver nanoparticles, have been used in household water filters. Current research on nanotechnology enabled water treatment has focused on four major areas: 1) Adsorptive removal of pollutants; 2) catalytic degradation; 3) disinfection and microbial control; and 4) membrane filtration and desalination (Li *et al.* 2008).

Nanomaterials can be superior adsorbents because of their extremely high specific surface area. Magnetic nano-adsorbents are particularly attractive as they can be easily retained and separated from water. The high adsorptive efficiency of magnetite nanoparticles can be used for removing heavy metals (e.g., arsenic) and radionuclides from water. The

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super-paramagnetic properties of nano-magnetite allow separation under low magnetic fields to enable recycling and reuse. This technology was selected by Forbes magazine as one of the top five nanotechnology breakthroughs of 2006, and is currently being tested by Rice University at the pilot scale in sand filters in the city of Guanajuato, Mexico.

Table 1. Opportunities for ENM in Water Treatment and Reuse

Desirable ENM Properties	Examples of ENM-Enabled Technologies
Large surface area to volume ratio	Superior sorbents with high, irreversible adsorption capacity (e.g., nanomagnetite to remove arsenic and other heavy metals)
Enhanced catalytic properties	Hypercatalysts for advanced oxidation (TiO_2 & fullerene-based photocatalysts) & reduction processes (Pd/Au to dechlorinate TCE)
Antimicrobial properties	Disinfection without harmful byproducts (e.g., enhanced solar and UV disinfection by TiO_2 & derivatized fullerenes), surface nanopatterning for biofouling control
Multi-functionality (antibiotic, catalytic, etc.)	Fouling-resistant (self-cleaning), functionalized filtration membranes that inactivate virus and destroy organic contaminants
Self-assembly on surfaces	Surface structures that decrease bacterial adhesion, biofilm formation and corrosion of water distribution and storage systems
High conductivity	Novel electrodes for capacitive deionization (electro-sorption) and low-cost, energy-efficient desalination of high salinity water
Fluorescence	Sensitive sensors to detect pathogens and other priority pollutants

Many nanomaterials have (photo)catalytic properties that can be used for oxidative or reductive degradation of chemical pollutants as well as disinfection. Potent bacterial and viral inactivation capacity has been demonstrated for functionalized fullerenes and TiO_2-based nanocomposites in the presence of visible and UV light (Lee *et al.* 2009). This approach represents a significant improvement over current chemical disinfection methods that produce harmful disinfection byproducts and are ineffective to disinfectant-resistant pathogens such as *Cryptosporidium* and *Giardia*. The same process can be used to treat recalcitrant pollutants such as pharmaceutical compounds and endocrine disruptors. Superior (hyper)catalysts, consisting of palladium-coated gold nanoparticles, have also been developed to promote rapid dechlorination of organic solvents such as trichloroethylene.

The remediation of groundwater contaminated by oxidized pollutants can be significantly enhanced by the use of nano-scale zerovalent iron (NZVI), a powerful reductant ($E_h° = -409$ mV) that can be used to dechlorinate TCE or reductively immobilize some heavy metals such as Cr(VI) or radionuclides such as U(VI). Pilot field studies have demonstrated the feasibility to inject NZVI into contaminated aquifers to create reactive zones or permeable reactive iron that intercept and destroy priority pollutants (He *et al.* 2010). NZVI is particularly attractive for source-zone remediation.

Biofilm formation in water distribution and storage systems harbors pathogens, causes biocorrosion and increases energy consumption. A promising approach to prevent these problems without formation of disinfection byproducts or use of toxic biocides is to create biofouling resistant surfaces by manipulating surface physical structures at the micro and nano scale, a mechanism used by marine organisms (dolphins and sharks) and plants (lotus leaf) to prevent bioadhesion. A combination of advanced photolithography, nanoparticle surface assembly and novel nano-template based methods could be used to create surface patterns that inhibit bacterial adhesion (Nel *et al.* 2009).

Development of multifunctional membranes is another area where nanotechnology may revolutionize water treatment. The application of membranes for drinking water and wastewater treatment is rapidly growing. Especially for areas where fresh water supply is

limited, the need for brackish ground water and seawater desalination as well as potable reuse of wastewater requires high-efficiency membrane systems. In spite of the advantages membrane systems offer, the inherent problem of membrane fouling, e.g., scaling, organic fouling and biofouling, poses the biggest obstacle to their broader application. In addition, the large plethora of contaminants in water and the diversity in their properties usually requires multiple stages of treatment. Incorporation of functional (e.g., adsorptive, (photo)catalytic and antimicrobial) nanomaterials into water treatment membranes offers the opportunity to achieve multiple treatment goals in a single step while protecting membranes from fouling. For example, when irradiated by low energy UV light, TiO_2 is bactericidal and can degrade a wide range of organic contaminants including natural organic matter, a major membrane foulant. Furthermore, controlled release of Ag^+ from Ag(0) nanoparticles can inhibit bacterial adhesion and growth (Yang *et al.* 2009; Zodrow *et al.*, 2009).

Nanotechnology could also help improve the energy efficiency of existing desalination technologies and develop novel, low energy consumption methods for desalination (Lind *et al.* 2009). Seawater is becoming an important source of water supply in many areas in the world. However, existing seawater desalination technologies are highly energy intensive. Utilization of nanomaterials (e.g., single wall carbon nanotubes) and biomaterials (e.g., aquaporins) has been explored to increase efficiency of membrane based desalination. Capacitive deionization (CDI) is a process that promises to provide a low-cost, energy-efficient technology for desalination. Removing salts by cation and anion electro-sorption in electrically conducting and porous electrodes, CDI avoids the high pressure required in RO and high temperature required in MSF, and provides high water recovery. The theoretically calculated as well as experimentally estimated energy consumption of CDI is more than an order of magnitude lower than RO. The current technology limitation lies in the low conductivity and low specific surface area of electrodes. We are developing novel electrodes with super high conductivity and surface area by employing vertically aligned carbon nanotubes, and evaluating their applicability for CDI of high salinity water.

Potential Risks to Human and Ecosystem Health

The nanotechnology revolution has a great potential to enhance not only water purification but also a wide variety of products, services, and industries. This promise, however, may be offset by the concern that some ENMs are toxic and may become a new class of hazardous pollutants that threaten public and ecosystem health if accidentally or incidentally released to the environment. Therefore, it is important to understand how released ENMs migrate, behave, and interact with living organisms and the abiotic components of the environment, and take proactive steps towards the long term goal of safer design and disposal of ENM-containing products (Klaine *et al.* 2008, Alvarez *et al.* 2009). Although the recognition of the environmental, health and safety issues of ENMs has been rising, research activities in this area are comparatively low, producing only about 5% of the total papers in environmental nanotechnology (Figure 1).
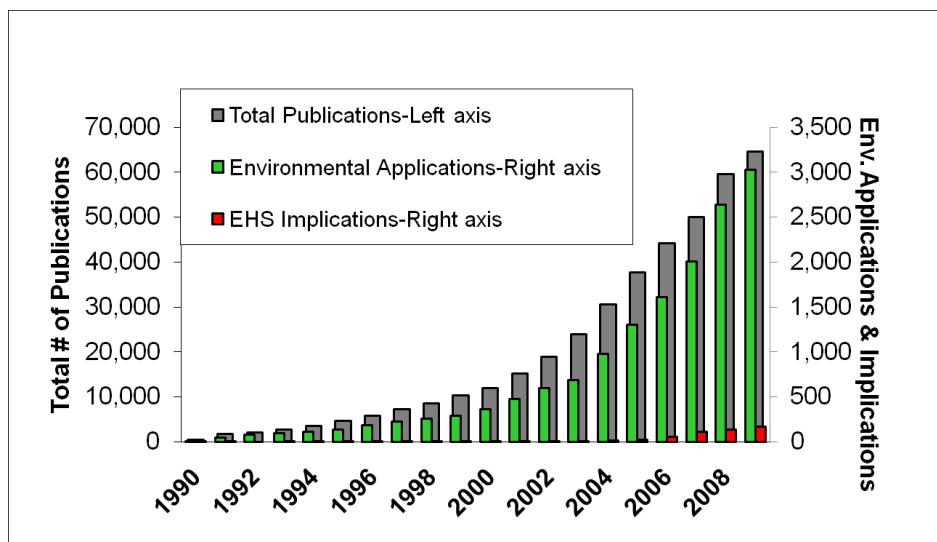
Figure 1. Comparison of the numbers of publications on environmental applications and implications (i.e., environmental health and safety, EHS) of nanotechnology (Source: ISI Web of Science, May 2010).

Whether ENMs could be designed to be "safe" and still display the reactivity or properties that make them useful is an outstanding question. Focusing on exposure control rather than suppressing intrinsic reactivity that contributes to toxicity might be appropriate in many cases. Thus, risk abatement options worthy of consideration include tailored coatings that reduce bioavailability or mobility, on-board packaging, and special disposal strategies. Yet, the modern chemical industry has demonstrated that some substances can be re-engineered to create safer, greener, and yet effective products. Encouraging examples include the substitution of branched alkylbenzene sulfonate surfactants, which caused excessive foaming in the environment, with biodegradable linear homologues, as well as the replacement of ozone-depleting chlorofluorocarbons by less harmful and less persistent hydrochlorofluorocarbons. Thus, it is important to discern the functionalities and physicochemical properties that make ENMs harmful, and determine which ecological receptors and ecosystem services might be at higher risks. Accordingly, priority research areas to inform the eco-responsible design and disposal of ENMs include:

1. Structure-activity relationships for ENMs in the environment. Modifying the physical and chemical properties of an ENM to affect its mobility, reactivity, bioavailability and toxicity.
2. Metrology, quantification and tracing ENMs. Analytical capabilities are needed to quantify ENMs in complex environmental and biological matrices (without alteration during separation and concentration) and determine the form that will reach receptors after they aggregate, dissolve, acquire/lose coatings, or undergo other transformations in the environment.
3. Bioavailability and sub-lethal effects. Standardized protocols are needed to investigate ENM cellular uptake mechanisms, trophic transfer and biomagnification potential (including discerning likely entry points into food webs) and sub-lethal effects that affect ecosystem services such as primary productivity, nutrient cycling, and waste degradation.
4. Predictive modeling of multimedia fate and transport. Computational models that predict the form and concentration of ENMs at the point of exposure will be important to identify the most susceptible compartments and ecological receptors and assess the associated risks.
5. Disposal scenarios and release dynamics. Immobilization and separation technologies need to be developed to retain ENMs in systems where their functions are desired. Meanwhile, sources and discharges into various compartments must be quantified (including ENM leaching from products)

as a first step to predict exposure and to evaluate the need for interception or remediation technologies.

Adopting principles of industrial ecology and pollution prevention should also be a high priority to steward ecologically-responsible nanotechnology (Table 2). Such measures can help the application of nanotechnology for sustainable water management while avoiding unintended impacts.

Table 2. The 12 Principles of Ecologically-Responsible Nanotechnology

1. Inherent rather than circumstantial (use raw materials and elements that are inherently non-hazardous if dissolved or otherwise released)
2. Prevention rather than treatment (containment, minimize exposure by choosing appropriate coatings, *design away hazardous functionalities or features without impacting useful functions*)
3. Design for separation and purification of nano construction wastes (take advantage of magnetic properties for separation /stabilizing coatings that can be intentionally removed after use to coagulated and precipitate MNMs /introduce surface properties to enable facile aggregation after environmental release)
4. Maximize mass, energy, space, and time efficiency (use multi-functional MNMs, quality > quantity, need > greed, enough >more, long-term > short-term)
5. "Out-pulled" rather than "input-pushed" through the use of energy and materials (drive manufacturing reactions to completion by removing products rather than increasing inputs of materials or energy, according to Le Châtelier's principle).
6. Find opportunities for recycle, reuse or beneficial disposition (non toxic NPs that enhance nutrient or water retention and soil fertility?)
7. Target durability rather than immortality (avoid indefinite persistence)
8. Need rather than excess - don't design for unnecessary capacity – avoid "one size fits all" (incorporate just what you need, avoid excess ENMs in commercial products)
9. Minimize material diversity to strive for material unification and promote disassembly + value retention (minimize variability and sources of a given ENM?)
10. Integrate local material and energy flows (holistic life cycle analysis perspective, look for interconnectivity, system of systems)
11. Design for commercial "afterlife" (enable recycling, remanufacturing and/or reuse opportunities, beneficial disposition)
12. Use renewable & readily available inputs through life cycle (minimize carbon, land use and water footprint)

Barriers for Implementation in Developing Countries

Insufficient technical capacity/knowledge needed to apply an advance technology might be an initial implementation barrier that could be relatively easy to overcome with an appropriate technology transfer program. This premise is supported by the widespread use of cell phones in developing nations.

Although the manufacturing costs of some ENMs (e.g., nano-magnetite) are predicted to be low in the near future, the current high cost of many ENMs is and may remain the main barrier for application in the water sector. Current costs of some ENMs are known (Table 3) but the cost normalized to the volume of water treated is unknown since their lifetime capacity (including recyclability) has rarely been tested to exhaustion. In addition, currently available cost information for many ENMs is based on small scale production and research grade ENMs. These complications preclude meaningful cost comparison with existing technologies. Despite the current high cost of nano-enabled products, their use in the water

sector is likely to increase at the point of use/entry scale because of (1) highly valuable properties imparted at relatively low additive ratios; (2) rapid development of new applications harnessing unique nano-scale properties; (3) decreasing trend in cost of nano-enabled products; and (4) save on capital investment for centralized infrastructure.

Table 3. Prices of Selected Nanomaterials of Interest to the Water Sector.

Zero Valent Iron, TiO_2 and Magnetite are currently available in (semi) bulk quantities. Others are more expensive research-grade materials.

Nanomaterial	Price (US$/gram)
Nano Zero-Valent Iron	0.14
Nano TiO_2	0.18
Nano Magnetite	0.44
Nano Iron-Oxide	1.20
Nano Silver	19.60
Fullerenes (C_{60})	330.00

Large-scale treatment plants can provide treated water at costs of as little as US $0.1 to $0.3 per 1,000 gallons of treated water over their life cycle. However, the initial capital cost of constructing the facilities is prohibitively large for developing countries (millions of dollars). Smaller point-of-use type treatment systems provide relative independence from extensive infrastructure and are much more reasonable in initial cost (on the order of US $100) but may require much higher operating costs of as much as $100 per 1,000 gallons treated for highly advanced point-of-use treatment systems. In order to be economically competitive in this cost range, current prices of nanomaterials would require that 1,000 gallons of water be treated by 200 g of titanium dioxide or 100 mg of fullerenes. As technology grows and prices of nanomaterials fall, this figure could become more realistic—especially in view of how many nanoparticles are in 1 gram of material.

Conclusions

ENMs have great potential to meet current and growing clean water demands throughout the world as the above-mentioned barriers are overcome. As the science and engineering of nanomaterials continue to grow, these improvements will likely come more and more rapidly. For instance the ability to use low cost, natural source materials and green manufacturing will reduce the environmental footprint and cost of nanomaterials. Additionally many of these technologies can take advantage of regeneration, reuse and recycling of ENMs to increase yield and further reduce cost. As the range and scope of pollution in water systems continue to increase we may see specialized treatment processes wherein nanotechnology can fill the gaps where conventional water treatment is either marginally effective or not feasible. Finally, efforts to control the release of ENMs into water systems will mitigate the environmental risk (and associated potential liabilities) until fate, transport and eventual impact of these materials are better understood.

Overall, it is important to capitalize on the leapfrogging opportunities offered by nanotechnology to improve and protect water quality. Furthermore, proactively assessing and mitigating potential environmental impacts of nanotechnology in the early stages of its development may result in better, safer products and less long-term liability for the industry. Indeed, due diligence is needed to ensure that nanotechnology evolves as a tool to improve material and social conditions without exceeding the ecological capabilities that support them.

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Annex II
Round Table 2 background paper and related mini papers

Round Table 2
Background Paper
Nanotechnologies in Agriculture: new tools for sustainable development
Hongda Chen, Vittorio Fattori, Masami Takeuchi, Rickey Yada

Outline

1. Science and Technology in Agriculture: opportunities and challenges for the developing World
2. Nanotechnologies in Future Agriculture
   2.1 Precision Farming and Other Nanotechnologies in Plant-Based Production
   2.2 Animal Production and Animal Health
   2.3 Nanotechnologies and Water for irrigation
   2.4 Nanotechnology for agricultural products distribution
   2.5 Nanotechnology and Traceability
   2.6 Nanotechnologies and clean energy
3. Good policies for fair and sound technological development
4. Need for partnerships and collaborations for sustainable agriculture development
5. Concluding remarks

1. Science and Technology in Agriculture: opportunities and challenges for the developing World

Agriculture sector today is facing growing global challenges: climate change, maximizing land-use in different environments, sustainable use of resources and minimizing negative environmental impact such as accumulation of pesticides and fertilizers. The situation is further exacerbated by the food demand for sustaining an estimated population growth from the current level of 6 billion to 9 billion in next forty years. In addition, considering the world diminishing petroleum resources, agricultural products and materials will soon be viewed again as the foundation of commerce and manufacturing.
At the same time there are new opportunities emerging. For example, the use of agricultural waste for the generation of energy and electricity could be one of them if the economics are ensured. This rapidly evolving and yet complex agriculture scenario is posing even more challenges to developing countries, where the agriculture sector and commodity production are the backbone of the economy, and where commodity dependence and poverty are closely intertwined.

Over the last several decades, the rapid growth and technological innovations have led to profound structural changes in the agriculture sector, including a transition from smallholder mixed farms towards large-scale specialized industrial production systems, a shift in the geographic locus of demand and supply to the developing world and an increasing emphasis on global sourcing and marketing. While all these changes pose significant challenges, they also have implications for the agriculture sector to a possible improvement of its production sustainability in ways that promote food security, poverty reduction and public health.

Advances in science and technologies could offer potential for developing countries to innovate and add value to their current commodities production systems, but once again, can also pose additional challenges. Many technologies being developed have the potential not only to increase farm productivity but also to reduce the environmental and resource costs sometimes associated with agricultural production. These include technologies that conserve land and water by increasing yields with the same or fewer inputs and technologies that protect environmental quality.
It will, therefore, be crucial to support these applications even if not commercially lucrative. At the same time there is also a need to avoid the risk that advances in science and technology increase the disparity between developed and developing countries. A serious consideration of the social and ethical implications on new agriculture technologies is thus necessary. While new agri-food technologies may deliver efficiencies in some areas, they may not necessarily solve existing problems of global food production and distribution. In this regard it is essential for developing countries to actively participate in research and development of new technologies. It is also important to consider strategies for science and technology innovation capacity building and establishment of relevant partnerships between developing countries and more advanced countries.

2. Nanotechnologies in Future Agriculture

Nanoscale science, engineering and technology embrace an exciting and broad scientific frontier which will have significant impacts on nearly all aspects of the global economy, industry, and people's life in the 21st century. Nanoscale sciences reveal the properties, processes, and phenomena of matters at the nanometer (1 to approximately 100 nm) range. Nanoscale engineering renders precise capability to control and/or fabricate matters at this length scale to render novel and useful properties thus leading to many novel applications of nanoscale science and nanomaterials that can be used to address numerous technical and societal issues.

In this section, some potential applications of nanoscale science, engineering and nanotechnology for agriculture production and related issues are discussed. Despite a wide-range industrial interest in this area, examples of available commercial products are few. Most applications are either in the R&D pipeline or at the bench top exploration stage, however, it is likely that the agriculture sector will see some large-scale applications of nanotechnologies in the future. Current industrial examples, if known, are indicated in the sections below.

2.1 Nanotechnologies in Plant-Based Agricultural Production and Products

Plant-based agricultural production is the basis for broad agriculture systems providing food, feed, fibre, fire (thermal energy), and even fuels through advancements in biomass conversion technologies. While the demand for crop yield will rapidly increase in the decades ahead, the agriculture and natural resources such as land, water and soil fertility are limited. Other production inputs including synthetic fertilizers and pesticides are predicted to be much more expensive due to petroleum reserve constraints. Precision farming is an important area of study to minimize production inputs and maximize agricultural production outputs for meeting the increasing needs of the world sustainability. Given that nanotechnology may allow for the precise control of manufacturing at nanometer scale, a number of novel possibilities in elevating the precision farming practices are possible.

- *Nanotechnology enabled delivery of agriculture chemicals (fertilizers, pesticides, herbicides, plant growth regulators, etc.):* Many nanoscale carriers, including encapsulation and entrapment, polymers and dendrimers, surface ionic and weak bond attachments and other mechanisms may be used to store, protect, deliver, and release by control of intended payloads in crop production processes. One of the advantages of nanoscale delivery vehicles in agriculture field applications is its improved stability of the payloads against degradation in the environment, hence maintain its effectiveness and reduce application quantity. It helps address agricultural chemicals run-off and alleviate the environmental consequence. The nanoscale delivery vehicles may be designed to anchor on the plant roots or the surrounding soil structure and organic matters. Controlled release mechanisms allow the effective ingredients slowly up-taken, hence, to avoid temporal overdose, reduce the amount of agricultural chemicals used, and minimizes the input and waste. Environmental consideration including precision farming can keep environmental pollution to a minimum.

- *Field sensing systems to monitor the environmental stresses and crop condition*: Nanotechnology may be developed and deployed for real time monitoring of the crop growth and field conditions including moisture level, soil fertility, temperature, crop nutrients, insects, plant diseases, weeds, etc.). Networks of wireless nanosensors positioned across cultivated fields provide essential data leading to best agronomic intelligence processes with aim to minimize resource inputs and maximizing output and yield. Such information and signals include the best times for planting and harvesting crops and the time and level of water fertilizers, pesticides, herbicides, and other treatments that need to be administered given specific plant physiology, pathology, and environmental conditions.
- *Nanotechnology enables the study of plant disease mechanisms.* The advancement in nanofabrication and characterization tools have enabled plant pathologic studies of physical, chemical and biological interactions between plant cell details and various disease causing pathogens. A better understanding of plant pathogenic mechanisms such as flagella motility and biofilm formation will lead to improved treatment strategies to control the diseases and protect production. For example, spatial and temporal studies of plant pathogenic xylem inhabiting bacteria have traditionally been conducted by monitoring changes in bacterial populations through destructive sampling techniques of tissues at various distances from inoculation sites. This approach seriously limits the information that can be obtained regarding colonization, biofilm development, and subsequent movement and re-colonization of new areas, primarily because the same region or sample site cannot be followed temporally. Micro-fabricated xylem vessels with nano-size features have been shown very useful to gain a better understanding of the mechanisms and kinetics of bacterial colonization of xylem vessels such that novel disease control strategies may be developed (Cursino, et al., 2009; Zaini, et al., 2009).
- *Improving plant traits against environmental stresses and diseases:* Biotechnological research has been focusing on improving plant resilience against various environmental stresses such as drought, salinity, and others. Genomes of crop cultivars are currently being extensively studied and gene sequencing is expected to become available within a decade (Branton, et al., 2008).
- *Lignocellulosic nanomaterials:* Recent studies have shown that nanoscale cellulosic nanomaterials can be obtained from crops and trees. It opens up a whole new market for novel and value-added nano materials and products of crops and forest. For example, cellulosic nano crystals can be used as light weight reinforcement in polymeric matrix as nanocomposite (Mathew, et al., 2009; Laborie, 2009). Such applications may include packaging, construction, and transportation vehicle body structures. A consortium led by North Dakota State University (NDSU) is currently engaged in a project to commercialize a cellulosic nano whisker production technology, developed by Michigan Biotechnology Incorporate (MBI) International, from wheat straw. The cellulosic nano whiskers (CNW) would then be used to make biocomposites that could substitute for fibreglass and plastics in many applications, including automotive parts.

As indicated earlier, nanosized agricultural chemicals are most in the research and development stage. NaturalNano, a start-up company in Rochester, N.Y., has found a way to use Halloysite, a naturally found clay nanotube, as a low cost delivery for pesticides to

achieve an extended release and better contact with plants. It is estimated that spreading pesticides in this manner could reduce the amount of pesticides applied by 70 or 80 percent, a significant reduction and cost of pesticides as well as less impact on water streams.

As reported by Cui in their mini-paper, China has aggressively developing nanotechnology based delivery of agricultural chemicals. He estimated these technologies will be deployed for field uses in next 5 to 10 years. Broad applications in crop production will largely depend on market demands, profit margin, environmental benefits, and policy in the background of other available technologies.

2.2 Nanotechnologies in Animal Production and Animal Health

Agriculturally relevant animal production (livestock, poultry, and aquaculture) provides the society with highly nutritious foods (meat, fish, egg, milk and their processed products) which have been, and will continue to be, an important and integral part of human diets. There are a number of significant challenges in animal agricultural production, including production efficiency, animal health, feed nutrition efficiency, diseases including zoonoses, product quality and value, by-products and waste, and environmental footprints. Nanotechnology may offer effective, sometimes novel, solutions to these challenges.

Improving feeding efficiency and nutrition of agricultural animals:

A critical element of the sustainable agricultural production is to minimize production input while maximizing output. One of the most significant inputs in animal production is feedstock. Low feeding efficiency results in high demand of feed, high discharges of waste, heavy environmental burden, high production cost, and competing with other uses of the grains, biomass, and other feed materials. Nanotechnology may significantly improve the nutrient profiles and efficacy of minor nutrient delivery in feeds.

Most animal feeds are not nutritionally optimal. Adding supplemental nutrients is an effective approach to improve protein and minor nutrient efficiency. Other digestive aids such as cellulosic enzymes can facilitate better utilization of the energy in plant based materials. Furthermore, minor nutrients and bioactives can help improve overall health of animals so that an optimal physiological state can be maintained. A variety of nanoscale delivery systems have been investigated for food applications. They include micelles, liposomes, nano-emulsions, bio-polymeric nanoparticles, subsumes, protein-carbohydrate nanoscale complexes, solid nano lipid particles, dendrimers, and others. These systems collectively have shown numerous advantages including better stability against environmental and processing impacts, high absorption and bioavailability, better solubility and disperse-ability in aqueous based systems (food and feed), and controlled release kinetics. (Chen et al., 2003). Self assembly process and thermodynamically stable structure require little energy in processing hence fits the concept of sustainability, therefore, nanoscale delivery can be used to improve feed nutritional profiles and feeding efficiency. In addition, the nanoscale delivery systems can also be designed for the use of veterinary drug delivery which protects the drug through GI tract, and allows for release at the desired location for optimal effect. These advantages help improve the efficiency by which animals utilize nutrient resources, reduce material and financial burden of the producers, and improve product quality and production yield.

Similar to food applications, the design of an appropriate nanoscale delivery system will require a full consideration of the effectiveness of its intended uses while preventing any adverse or unintended effects. The nanoscale particles should be subject to a rigorous risk assessment. For a full discussion of nanoparticle safety, please refer to the same subject in Roundtables 1 and 3.

Minimizing losses from animal diseases, including Zoonoses

Many animal diseases cause substantial losses in agricultural animal production. Some of more significant diseases include bovine mastitis, tuberculosis, respiratory disease complex, Johne's disease, avian influenza, and porcine reproductive and respiratory syndrome (PRRS). The World Health Organization (WHO) estimates that animal disease represents as much as 17 percent of animal production costs in the developed world, and more than twice this figure in developing nations. On average, one newly identified animal infectious disease has emerged each year for the past 30 years of which approximately 75 percent have been zoonotic (*e.g.*, mad cow disease; Avian influenza; H1N1 Influenza; Ebola virus; Nipah virus). Zoonotic diseases not only cause devastating economic losses to animal producers, but also impose serious threats to human health. Detection and intervention are two important tools of an integrated animal disease management strategy that is critical to significantly reducing losses/threats from the target disease, and/or eradicating disease, or preventing disease introduction into the animal production. Nanotechnology has not only the potential to enable revolutionary changes in this area, but will be feasible in near future given the current state of science. Nanotechnology offers numerous advantages in detection and diagnostics including high specificity and sensitivity, simultaneous detection of multiple targets, rapid, robust, on-board intelligence, signal processing, communication, automation, convenient to use, and low cost. The use of portable, implantable or wearable devices are particularly welcome in agricultural field applications. Early detection is imperative in order that quick, simple and inexpensive treatment strategies can be taken to remedy the situation. Nanotechnology based drugs and vaccine can be more effective in treating/preventing the diseases than current technologies, thus reducing cost. Precise delivery and controlled release of nanotechnology enabled drugs leave little footprint in the animal waste and the environment, which alleviate the increasing concern of antibiotic resistance issue, and decrease health and environmental risks associated with the use of antibiotics. The targeted delivery and active nanoparticles may enable new drug administration that is convenient, fast, non-intrusive to animals, and cost effective. Theragnostics – a new generation of smart treatment combining diagnostics and therapy in a single step via nanotechnology – will further improve disease treatment efficiency and cost, and eliminate the diseases at early stage, even pre-clinically. While the effectiveness of new drug delivery technology platforms are being explored, the responsible development of new drug(s) should also be thoroughly investigated. The transport, fate and action mechanisms *in vivo* should be fully examined before a new drug delivery system can be deployed. Research and development for dealing with zoonotic diseases should collaborate with expertise from the human medical community for a more effective advancement.

Animal reproduction and fertility:

Animal reproduction remains a challenge not only in developed countries, but also in developing countries. Low fertility result in low production rate, increase financial input, and

low efficiency of livestock operations. Several technological fronts have been explored in order to improve animal reproduction. Microfluidic technology has matured as nanotechnology has developed over the last decade, and has been integrated into many nanoscale processing and monitoring technologies including food and water quality, animal health, and environmental contaminations. The development of efficient microfluidic technologies enables the automation of production of large numbers of embryos in vitro, which speed up the genetic improvement and selection of superior livestock for human food and fibre production.

Brazilian animal scientists have used Fixed-Time Artificial Insemination technology to effectively increase the cattle reproduction rate (Hoffman, et al., mini-paper) for many years. However, the technology depends on the regulation of progesterone administered through a silicone matrix. The procedure has significant drawbacks including inefficient and irregular dispersion of hormone, as well as issues related to disposal and being labor intensive requiring multiple animal handlings for each attempt. Nanoscale delivery vehicles are sought to significantly improve bioavailability and better control of release kinetics, reduce labor intensity, and minimize waste and discharge to the environment.

Another strategy that may be explored is to monitor animal hormone level using implantable sensing device with wireless transmission capability, thus the information of optimal fertility period can become available in real time to assist the livestock operators for reproduction decision making.

Animal product quality, value and safety

Modification of animal feeds has been effectively used to improve animal production and product quality and value. The regulation of nutrient utilization can be used to enhance the efficiency of animal production, and to design animal-derived foods consistent with health recommendations and consumer perceptions. For example, the concept of nutrient regulation have been used to redesign foods, such as milk fatty acids, cis-9, trans-11 conjugated linoleic acid (CLA) and vaccenic acid (VA), that have a potential role in the prevention of chronic human diseases such as cancer and atherogenesis. The biosynthesis and concentration of CLA and VA in milk fat of lactating ruminants can be enhanced and better controlled by nanotechnology enabled delivery of nutrients. Collaborative research examining the biological benefits of functional foods with enhanced CLA/VA content in biomedical studies with animal models of human diseases and in human clinical using biomarkers for chronic disease could benefit from new tools based on nanotechnology capabilities. Biomarker triggered release mechanisms may be explored for new discoveries of nanoscale structural actions.

Biotechnology has been explored also in animal and food product quality. Nanotechnology research is attempting to sequence a mammalian genome in less than 24 hours and less than $1000.

Turning animal by-products and waste and environmental concerns into value added products

Animal waste is a serious limiting factor in the animal production industry. Stricter environmental policies prevent irresponsible discharge of animal waste. Unpleasant smell adversely affects air quality, and in turn, living conditions and real estate value of the

adjacent area. However, value added uses through bioconversion of animal waste into energy and electricity will result in revenue, renewable energy, high quality organic fertilizer, and improving environmental quality. Nanotechnology enabled catalysts will play a critical role in efficient and cost effective bioconversion and fuel cell for electricity production. Nanotechnology enabled efficient energy storage will greatly facility the development of distributed energy supplies, hence especially beneficial to rural communities where infrastructure is lacking. Such an approach may result in the elimination of system wide electricity grids, hence accelerate the rural development and improve productivity, and business and living environment.

2.3 Nanotechnologies for Water Quality and Availability

Providing clean and abundant fresh water for human use and industry applications is one of the most daunting challenges facing the world. It is estimated that "more than one billion people in the world lack access to clean water, and the situation is getting worse. Over the next two decades, the average supply of water per person will drop by a third, possibly condemning millions of people to an avoidable premature death" (Savage, et al., 2009). Agriculture requires considerable amount of fresh water and in turn, often contributes significantly to pollution of groundwater through the use of pesticides and fertilizers. Considering the volume of wastewater produced by farms on a continual basis, any technology for remediation and purification will need to be able to manage the volumes and be cost effective.

Technical issues in the water challenges include water quality and quantity, treatment and reuse, safety due to chemical and biological hazards, monitoring and sensors. Nanotechnology R&D has shown great promises to provide novel and economically feasible solutions. Several aspects of nanotechnology solutions are briefly discussed below.

Water quantity, quality and safety – Treatment, Decontamination, Reuse, and Conservation

Accessible water resources are often contaminated with pollutants largely due to various human activities, but also natural leaching. These contaminants include, but not limited to, water-borne pathogenic microorganisms (*Cryptosporidium*, coliform bacteria, virus, etc.), various salts and metals (copper, lead), run-off agricultural chemicals; tens of thousands of compounds considered as pharmaceuticals and personal care products (PPCP) and endocrine disrupting compounds (EDC), and radioactive contaminants either naturally occurring or the result of oil and gas production and mining activities. For drinking water, sensory attributes (taste, smell, turbidity) are also important quality indicators. Various nanoscale tools have been explored to address these challenges to improve water quality and safety (for nanotechnology applications and drinking water see also mini-paper by Dr Pedro Alvarez).

Microbial disinfection: In the industrialized nations, chemical and physical based (chlorine dioxide, ozone, and ultraviolet) microbial disinfection systems are commonly used. However, much of the world still does not have the industrial infrastructure to support chemical-based disinfection of water. Hence, alternative technologies that require less

intensive infrastructure and more cost effective approaches such as nanoscale oligodynamic metallic particles may be worthy of attention. Among the oligodynamic metallic nanoparticles, silver is considered the most promising nanomaterials with bactericidal and viricidal properties owing to its wide range effectiveness, low toxicity, easy to use, its charge capacity, high surface to volume ratios, crystallographic structure, and adaptability to various substrates (Nangmenyi and Economy, 2009). Its antimicrobial mechanism may be its production of reactive oxygen species (ROS) that cleaves DNA. Another nanotechnological development for microbial disinfection is visible light photocatalysts of transition metal oxides made into nanoparticles, nanoporous fibers, and nanoporous foams (Li et al., 2009). In addition to its effectiveness in disinfecting microorganisms, it can also remove organic contaminants such as PPCPs and EDCs). CNT may be embedded into microbial cell wall to disrupt its structure integrity and resulting in leakage of intracellular compounds.

Desalination: Given the limited fresh water supplies both above or under-ground, treatment of sea and salty water of fresh water is inevitable in the not-too-distant future. Conventional desalination technology is reverse osmosis (RO) membranes which generally require high energy for operation. A number of nanotechnologies have been attempted to develop low energy alternatives. Among them, protein-polymer biomimetic membranes, aligned-carbon nanotube membranes, and thin film nanocomposite membranes are three promising examples (Hoek and Ghosh, 2009). Some of the prototypes have demonstrated up to 100 times better water permeability with nearly perfect salt rejection than RO. CNT membranes, owing to its extremely high water permeability than other materials of similar size, have desalination efficiencies in the order of thousand times. Some these membranes can also integrate other functionality such as disinfection, de-odor, de-fouling, and self-cleaning. Technical challenges such scale up fabrication, practical desalination effectiveness, and long-term stability must be addressed before a successful commercialization. Some of the above mentioned technologies are in commercial development stage, which may be introduced in the market place in near future.

Removal of heavy metals: Functionalization of ligand-based nanocoating which is bonded to the surface of high surface and low cost filtration substrate can effectively adsorb high concentration of heavy metal contaminants. The system can be re-generated in situ by treatment with bifunctional self-assembling ligand of the previously used nanocoating media. A start-up company Crystal Clear Technologies has demonstrated that such a multiple layers of metal can be bonded to the same substrate (Farmen, 2009). Such water treatment unit should be available in near future for removal of various heavy metals in water. Another approach to remove heavy metals and ions is to dendrimer enhanced filtration (DEF) (Diallo, 2009). Functionalized dendrimers can bind cations and anions according to acidity.

Water conservation in agricultural crop production: The fact that crop production uses large amount of water has triggered the implementation of policy and regulations in limiting agricultural production in many regions. Scientists and engineers have been working to improve water usage conservation in agricultural productions. For example, drip irrigation has been developed for many crop productions to conserve water. This innovation has move precision agriculture in water used to a much higher grand than other irrigation technologies such as flood irrigation. New ideas will likely result in the development of precision delivery systems of water. Technology platforms that may be considered include water storage, in

situ water holding capacity, water distribution near roots, water absorption efficiency of plants, encapsulated water release on demand, interaction with field intelligence obtained through distributed nanosensor systems, and others that have not been imaged before.

Detection and Sensing for Pollutants and Impurity

Nanotechnology based sensor and detection of various contaminants in water have been a hot topic over the last decade. Detection level is at parts per billion (ppb) for metals and organic contaminants for both laboratory and field applications. The state of science and prototyping for sensing and devices is among the most advanced in the field of nanotechnology, hence it is expected many technologies will be readily available in the next decade. Sensor applications for water bear many similarity to other applications, hence are not repeated here. For the general discussion on sensors, please refer to other sections of this paper for more details.

2.4 Nanotechnology for agricultural products distribution

Many agricultural products are perishable or semi-perishable. These include fresh produces, fruits, meats, egg, milk and dairy products, many processed foods, nutraceuticals and pharmaceuticals, etc. The improvement of shelf-life is one of the main areas is a current area of focus for nanotechnology research to enhance the ability to preserve the freshness, quality and safety (see Roundtable 1 Backgrounder and mini-papers).

2.5 Nanotechnology and Traceability

A number of factors contribute to an increased demand for the traceability of foods throughout production, processing, and distribution. Food safety outbreaks frequently resulted in wide spread product recall. Advanced and improved product traceability is essential to ensure food safety in the recall process. Also, product authenticity has an increased value in food marketing throughout the world by validating the origin, and therefore, the unique inherent value of the products.

Traceability must meet the following five essential technical challenges (Nightingale, 2008):
1. Enough vocabulary
2. Not compromise the product
3. Same life as the product service life
4. Easy to read
5. Very inexpensive

In response to this market-driven requirement, several systems have been developed to provide consumers with information about the origin of agricultural products and the practices used to produce those products. Dr. Luo at Cornell University has developed nucleic acid engineered nanobio barcode technology. It meets all the five requirements. It has been tested in identifying non-point pollution sources in underground hydrological pathways. It has potential to be used in foods and many other traceability applications.

Nanotechnology-based tracing devices can integrate multiple functional devices that provide other important information such as sensors for detection of the presence of pathogens, spoilage microorganisms, chemicals, and other contaminants in food as well as nutritional information. Additionally, nanoscale tagging devices can be used to record and retrieve information about the product history. These types of applications will aid producers, retailers and consumers regarding food safety, food quality, and other standards, e.g., nutritional information

A challenge in new technology development is to manage the cost to be acceptable for its intended use. The inability to manage this cost will pose additional barriers for many developing countries in exporting their products, as this will require for more detailed and sophisticated information about their agricultural products traceability. Fortunately, the inherent advantage of nanomanufacturing of precise and minimal use of materials, hence may reduce the production cost is on the side of cost control.

2.6 Nanotechnologies and clean energy

Access to inexpensive, safe and renewable energy is an important issue for sustainable development worldwide. Flexible and efficient, yet inexpensive solar cells are often highlighted as one of the most exciting areas of nanotechnology application in agriculture, as often expressed as "green nanotechnology." Inexpensive type of solar-powered electricity has long been an aspiration for tropical countries, but glass photovoltaic panels remain too expensive and delicate. Nanotechnology based photovoltaic currently is a high priority of research worldwide, including the most industrialized countries. Other nanotechnology for solar energy conversion to electricity, energy storage, and nanotechnology enhance solar thermal energy systems are presently active areas of research and development. Cost reduction in photocatalysts and energy materials is in the core of the research. As the research and development advances, the economic feasibility and hurdles of photovoltaic technologies will become clearer; hence strategies may be developed to properly address them. More and more out-of-box ideas, such as the use of photosynthesis protein units in leafy vegetables and plants to directly convert solar energy to electricity (Jennings and Cliff, 2008), will emerge to greatly enrich our tool box. Harnessing solar energy will be a grand challenge that benefits humanity, hence the pursuit will be persistent and intensive in next few years.

Nanotechnology can also contribute to conversion of biomass for fuels, chemical intermediates, speciality chemicals and products. As biomass becomes an increasingly important industrial feedstocks, a new generation of catalysts to reduce production cost and make it economical feasible is critically important. Nanostructure is inherently advantages as catalysts due to its large surface area per unit volume, and newly developing capability to precise control composition, structure, functionalization, and other important properties of catalysts.

3. Good policies for fair and sound technological development

Nanotechnology, as has been commonly defined, i.e., 1- 100nm, has been actively pursued in the world for about ten years. While many advances have been made, the development has been inconsistent in some areas. In agriculture, the research is still in its infancy. While the potential for many beneficial applications have been demonstrated at concept and bench top, greater efforts are required for commercialization. At the same time, research on methodology, identification of materials, testing priorities and regulatory guidance on nanoparticle safety is also at its infancy. Increased research funding, including benefits and potential risk for responsible development, is required to move the field forward. To effectively achieve it, all the stakeholders should be engaged. Private-public partnership (PPP) will help effectively advance the sciences. The public should be engaged in a transparent and constructive forum to discuss all concerned issues.

Good polices should also focus on funding research and development, technology transfer activities, and efforts to understand and facilitate technology adoption and sharing among industrialized and disadvantage countries.

Addressing all these issues in relation to nanotechnology innovation and development means to:
- Enhance the role of developing countries in responsible nanotechnology development;
- Encourage the development of appropriate products targeted to help meet critical human development needs;
- Include methods for addressing the safety, appropriateness, accessibility and sustainability of nanotechnology to meet the needs of developing countries.

4. Need for partnerships and collaborations for sustainable agriculture development

Nanotechnology by its very nature will and has required a high degree of multidisciplinary and cross-sect oral collaboration within and between academic researchers and industry. Applications of nanotechnology involves many disciplines in engineering and the natural sciences, including physics, chemistry, biology, materials sciences, instrumentation, metrology, and others. As nanotechnology progresses from discovery to potential applications, it requires a number of tools for visualization, characterization, and fabrication, as well as methods for reproducing and controlling properties, scalability, and cost. These tools and techniques, too, are typically rooted in multiple disciplines.

Despite progress in developing countries with strong research capacities, many developing countries continue to work on filling these gaps in infrastructure through contact and access to international research and development networks and seek missing linkages between the public sector research community and industry. Therefore, it is important to undertake an evaluation of possible collaboration and partnership mechanisms either between public and private or between developed and developing countries to continue meeting global demands and expectations in this field. Several developing countries are already investing strategically and conducting research in nanotechnology applications for agriculture. In particular, Brazil, China, India, and South Africa have been noted for their significant investments in nanotechnology research and development and the development of national

nanotechnology strategies focusing on areas of national interest including energy, health, water treatment, agriculture, and environment.

The combination of public-private-sector partnerships and developed-developing countries collaborations will be useful in achieving new goals in agricultural development ultimately resulting in mutual and global benefits. In doing so, there are some key aspects that might need particular attention:

- Exploring new ways of working with the agriculture industry by developing alternative activities that are of benefit to industry and the country where the industry operate
- Developing and promoting regulations that can stimulate private-sector research in fields of common interests both to the public and to the industry. For example, incentives attempting to protect the environment, food safety, and nutrition may encourage research on technologies that are more compatible with social as well as business goals.
- Education and workforce training are essential in enhancing scientific capabilities in all nations. Numerous courses, workshops and conferences are organized by academia, professional societies, governments, and private entities. Young scientists and students should take the advantage of these offerings to acquire new knowledge and skills required to be proficient workers and researchers in nanotechnology. One of the most recent examples is the International Conference of Food Applications of Nanoscale Science held in Tokyo from June 8-10, 2010. A number of graduate students and young scientists from developing countries participated to learn from plenary session presentations, presenting their research posters, and interacting with the leading scientists from around the world.
- To accelerate research in nanotechnology in agriculture, an increased intensity of investment is absolutely needed. Government funding agencies, agriculture and allied industries, venture capitals, and other financial institutes should consider investing in R&D in it as the agriculture and renewable production will be central to global sustainability and will require intensified investment to develop technical capabilities for solutions to numerous technical challenges ahead.
- International cooperation is germane and essential in an ever increasing globalized economy. Each country has limited resources to invest in research and education. All standing, therefore, working in a complementary manner and combining resources will allow for the effective advancement in nanoscale science and responsible development and deployment to the benefit of society. International organizations such as UN/FAO, WHO, IUFoST, and others should promote and facility international exchanges and cooperation. Most recently, the IUFoST has tentatively accepted a proposal to form International Society of Food Applications of Nanoscale Science (ISFANS), with its vision to "to strengthen research, communication, dissemination of information and networking for technology transfers and international collaborations among interested parties from academia, industry, government, consumers, and other participants around the world. " This is one of many ways to effectively promote and improve international cooperation. Governments can also help bilateral and multilateral scientific cooperation through their respective MOUs. Academia has long history of collaboration internationally through joint research and training graduate students and postdoc fellows. All these should be encouraged.

5 Concluding remarks

The intent of this backgrounder is to provide an overview of agriculture "nano" applications in order to share common understanding of the current situation around the topic and to base recommendations and strategies for moving forward on the best scientific knowledge presently available.

During the roundtable sessions, participants and participants will be asked to identify: potential benefits; implications for human and environmental health; challenges (including technical, financial and capacity-related challenges); as well as opportunities and strategies for developing countries to gain the expected benefits. In addition to this identification process, it is important that the participants and participants also identify and suggest possible mechanisms for partnerships and collaborations (e.g. between developed and developing countries, public-private, between research institutions and international organizations etc), which will be incorporated into the final report of this event.

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Title: Nanomaterials for Renewable Energy
Name: Prof.(Dr.) Kuruvilla Joseph [34]

Introduction

Availability of energy at low cost is key to the development of any nation. However, over dependency on fossil fuels not only made them scarce but also resulted in global warming. One way to get out of this misery is to increase our dependency on renewable energy sources. Renewable energy sources such as hydroelectricity, electricity from wind, tide, bio-mass, geothermal energy and solar light already proved their capability. However, their share in the total energy is very low.

Large scale tapping of solar energy with photovoltaic technology is the most viable way to increase the share of renewable energy. The single crystal silicon photovoltaic technology, having low conversion efficiency, limits widespread usage. Nanomaterials and nanotechnology have already shown the way to improve the efficiency to a remarkably high value.

Key issues to be discussed

Supercapacitors, solar cells and fuel cells with improved efficiency using nanotechnological advancements. Due to greater energy density than those of conventional capacitors and greater power density than batteries; supercapacitors have kindled the interests of the researchers in this field of energy storage. As a result, supercapacitors have become an attractive power solution for an increasing number of applications. Various nanocomposite materials are the focus of attention in developing multifunctional electrode materials for high power super capacitor applications. CNT is an excellent electrode material for supercapacitor application because of its high electrical conductivity, large surface area, polarizability, chemical and thermal stability. Utilization of Carbon nanotube (CNT) is an excellent electrode material for super capacitor application because of its high electrical conductivity, large surface area, polarizability, chemical and thermal stability. Fine tailoring of the nano-scale attachment of the electrode material that would definitely result in optimal performance in terms of energy, power, and cycling capabilities, demonstrating exceptional capacitance behavior and long-term chemical stability potentially suitable for numerous applications.

Fuel cells have the potential to serve a wide range of applications, including portable, stationary, and transportation power. Of particular interest is the portable power sector for commercial applications, such as portable electronics, and military applications in, for example, unmanned systems. As these applications increase in capability, power consumption increases and device operating time decreases. Since a fuel cell power source can provide extended operating time or instant recharge, it is an excellent candidate for use in high performance electronics. Researchers are using nano-sized catalysts to vastly improve the

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production of hydrogen through water electrolysis a vastly more efficient process. Efficient processes for hydrogen production are required, to pave the way for hydrogen as the future energy carrier,. Nanostructuring helps increase efficiency of precious metal catalysts in the electrolytic decomposition of water.

Challenges identified

Portable fuel cells typically use hydrogen or methanol as a fuel source. Direct methanol fuel cells (DMFCs) are attractive because the fuel can be stored as a liquid, whereas hydrogen fuel would need to be stored as a compressed gas or in the solid state as a hydride for a hydrogen fuel cell. Finally, the most common catalyst used in DMFCs is platinum, a precious metal that is expensive and limited in supply.
Carbon nanotubes (CNTs), with excellent electrical conductivity and high surface areas, have been fabricated for supercapacitors. Despite the advantages, the specific capacitance of pristine CNT is mediocre (< 40 F/g).

New generation photovoltaic cells based on nanomaterials, such as quantum dots and carbon nanotubes, have shown excellent performance in the laboratory scale. However, novel processing technologies has to be developed for the mass production of photovoltaic devices based on the nanomaterials. Photovoltaic cells based on organic nanomaterials have also been demonstrated. Though photovoltaic cells based on organic and polymeric materials have advantages with respect to ease of fabrication, they also have very low conversion efficiency. A tremendous amount of effort has to be put into improving the efficiency of organic photovoltaic cells.

Strategies to overcome the challenges
Approximately 20 - 30% of a DMFCs cost is related to high platinum loading. To bring down the price of the fuel cells, it is probable that costly platinum metal would be replaced with cheaper nanomaterials, resembling platinum chemically, like palladium.However, CNT-based supercapacitors have not met expected performance; one possible reason is probably due to the observed contact resistance between the electrode and current collector. Hence, many studies have focused on the morphology of the carbon materials to boost the performance of the capacitor, such as growing CNTs directly on bulk metals to eliminate contact resistance. The fine tailoring of the nanoscale attachment of the electrode material will definitely result in optimal performance in terms of energy, power, and cycling capabilities. Methods to improve the CNT capacitance via mixing with pseudocapacitive materials like MnO_2 have been reported. Due to their unique structural and electrical properties, carbon nanotubes (CNTs) have been extensively investigated as promising catalyst supports to improve the efficiency of direct ethanol/methanol fuel cells. CNTs have a significantly higher electronic conductivity and an extremely higher specific surface area in comparison with the most widely-used carbon support. Several approaches, such as electrochemical reduction, electroless deposition, spontaneous reduction, sonochemical technique, microwave-heated polyol process, and nanoparticle decoration on chemically oxidized nanotube sidewalls, have been reported to form CNT-supported platinum catalysts. Some remarkable progress has been made in synthesis techniques; however, pioneering nanotechnology breakthroughs have not been made yet in terms of cost-effectiveness catalyst activity, durability, and chemical-electrochemical stability. Nanotechnology researchers have now discovered that platinum nanoparticles selectively grow on carbon nanotubes in accordance with single-stranded DNA (ssDNA) locations. They have demonstrated that not only can ssDNA bind to nanotube surfaces, but

they can also disperse bundled single-walled carbon nanotubes (SWCNTs) into individual tubes. This finding suggests a method to synthesize other types of carbon nanotube-supported nanoparticles, such as palladium and gold for applications in fuel cells and nanoscale electronics. The major problems hampering the development of CNT-supported platinum catalysts are the lack of reliable approaches for controlling morphology, size, density, and configuration of platinum nanoparticles along carbon nanotubes.

Nanotubes tend to form bundles due to hydrophobic interactions in aqueous solutions and strong inter-tube van der Waals interactions. Consequently, most reported attempts have been limited to multi-walled carbon nanotubes (MWCNTs) and bundles of SWCNTs. SWCNTs are expected to have better characteristics as catalyst supports due to their larger surface area and smaller diameters. A desirable approach to producing platinum nanoparticles on SWCNTs must include two processes: the separation of bundled SWCNTs into individual tubes and the synthesis of platinum nanoparticles on the nanotubes.

Tuning of the nano rods to absorb various wavelengths of light could significantly increase the efficiency of the solar cell because more of the incident light could be utilized. Another major revolution that is likely to be executed within a few years is the possibility of the widespread use of solar cells based on quantum dots. Quantum dot based solar cells represent a milestone to breaking efficiency limits through use of nanomaterials.

Conclusion

One of the most feasible ways to overcome the present energy crisis is to achieve quantum leap processing in harvesting renewable energy resources. Energy harvesting, storage and energy management is to be carried out using clean energy sources. The goal is to make it practical and cost-effective to produce hydrogen from water and electricity for existing industrial uses and for fueling the next-generation hydrogen-fueled vehicles. Fabrication of highly reactive catalytic nanoparticle coatings could increase the efficiency of electrolysis, and the coatings could also eliminate the need for expensive metals like platinum in hydrogen fuel cells. Detailed information about the shipping environment is of special interest for perishable goods supply chains. Control and visibility over product handling is limited due to several echelons of the supply chain. Currently, battery-powered devices are used to monitor the shipping environment of goods in a cold chain but the cost of these devices, their bulkiness, and their limited lifetime prevent high market penetration. As a result, only limited information is available about the cold chain, which precludes useful insights as to its efficiency. Currently with the advance of nanotechnology there is a possibility of using nanosensors to track the cold chain and thus make the storage system more efficient. The insertion points for nanotechnology in sensing applications are many. Nanotechnology has the potential to enable the vision of future sensor technology and sensing systems. The high surface to volume ratio of nano wires and other nonmaterials add to increasing the sensitivity of the transducer in the sensor. Market potentials of nanotechnology in the energy conversion sector will mainly arise in the field of thin layer solar cells and in fuel cell technology. Apart from potentially low production costs and a more flexible scalability, thin layer solar cells bear the advantage of more consistent performance- even at fluctuating temperatures and sub optimum radiation conditions (angle of incidence, clouds). This opens up new application fields like flat roofs or extensive solar plants.

Title: Nanoparticle-based drug delivery for hormones: new tools for pharmacological control of the estrous cycle in ruminants.

Name: Ed Hoffmann Madureira[35], Lúcio Cardozo Filho

Introduction

Nanotechnology is a relatively new area of science and several authors have suggested its application in various fields of animal production and health. In order to enrich the discussions, several publications such as EMERICH; THANOS (2006), NARDUCCI (2007), SCOTT (2007) and KUZMA (2010) may be consulted.

The management of animals can be relatively difficult when there's a need to administer many different medications. Therefore, there's always been a need for formulations that allow a sustained release of the active ingredients, specially antimicrobials, anti-inflammatories and hormones. This can be achieved with the application of nanotechnology.

Another field of use would be in vaccines where it could improve the immune response through the continuous stimulus of the immune system.

The already available so-called long-acting drugs do not have adequate pharmacokinetics, which exposes the animals to excessive concentrations of the active ingredient in the beginning of the treatment and many times, concentrations below the therapeutic dose by the end of the treatment.

As a rule, drugs considered as long-acting have very aggressive vehicles and employ inadequate pH ranges for intramuscular administration, leading to local lesions at injection sites, responsible for an inferior meat quality.

Key issues

Brazil is one of the largest producers and exporters of beef in the world and the cattle herd consists of approximately 200 million heads of cattle. Of these, about 70 to 80 million are females of reproductive age. There are many challenges to improve reproductive performance and still get a genetic improvement in the breeding herd. For this, Artificial Insemination is an essential tool.

Our area of expertise is the pharmacological control of the estrous cycle, with the goal of synchronization of ovulation in cows in order to enable Fixed-Time Artificial Insemination (FTAI). The use of FTAI has provided a significant increase in the production of beef and dairy cattle and it has been widely used in producing countries. In Brazil, it has been estimated more than 3 million FTAI in the last year.

Among the main limitations for FTAI, in which nanotechnology could be useful, are: a) the animals must be managed 3 to 4 times until the moment for artificial insemination, b) the products used are based on progesterone dispersion in a silicone matrix and, after its use, a considerable amount of hormone residue in the devices that have to be discarded remains, c) the release of progesterone from these devices, although acceptable, is irregular, d) the devices must be removed from the vaginal cavity at the end of the treatment period, which leads to having to handle the animal one more time.

Challenges identified

To circumvent the limitations listed above, the main challenges are:

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a) the improvement of the bioavailability of progesterone, providing better control of the dose, b) the development of more appropriate formulations for different animal categories – heifers, dairy and beef cows have different progesterone requirements, c) the formulation of new veterinary medications in which progesterone content runs out by the end of the treatment to avoid the need for its removal, handling and disposal after use.

Strategies to overcome the challenges

In order to develop new formulations, a production of nanoparticles with polymers that have certain properties (such as biodegradability and biocompatibility) is necessary. It is indeed very important to select the most appropriate technique among those actually available (i.e. emulsification/solvent evaporation, emulsification/solvent diffusion, miniemulsification/evaporation or solvent extraction and nanoprecipitation (or displacement of solvent)) to establish an ideal loading and releasing efficiency rate for each individual drug and to allow large scale production in an economically feasible way.

As strategies to overcome these challenges a modification of polymeric materials by manipulating the biocompatibility and biodegradability of the synthetic nanoparticles polymers, and use of hybrid natural/synthetic polymer that offers new possibilities are needed. It is expected that the drug release will also be influenced by the composition of particles and by how these polymers interact with each other and with the drug. So the introduction of stabilization techniques combining new surfactants and physical processes (such as ultrasound) will also need to be considered.

Once a series of materials and methods is available for the production of nanoparticles, the need for the development and validation of analytical techniques for testing of nano-structured formulations, both "in vitro" and "in vivo" becomes essential. For "in vitro" tests, there is a need for standardization of delivery systems, adjustment of the formulations, stability and quality control tests.

The "in vivo" tests should also be emphasized, because if the formulations can provide improvements in the bioavailability of active ingredients and reduce meat and milk residue, then there's a need for analytical techniques sensitive enough to differentiate the traditional formulations from the nano-structured. Validation of techniques for measurement by mass spectrometry (LC /MS /MS) in different matrices such as blood, meat, milk, fat and other specific organs, becomes imperative.

Conclusion

In the area of animal reproduction, there is enough information on the physiology of the endocrine system and great interest for veterinary medications, which can be used to improve the reproductive performance of beef and dairy herds. In parallel, there is enough information on material engineering, production techniques and characterization of nanoparticles as well as "*in vitro*" and "*in vivo*" testing of nanostructured formulations.

It can be concluded that basic research already holds significant expertise in nanotechnology to generate in the short term, major technological products. This is happening in a peculiar economic moment in which there is increasing demand for effective products that can contribute to sustainable livestock development and at the same time meeting the requirements of animal welfare, consumer and environment safety.

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Title: Nanotechnology in agriculture: increasing pressure on small scale farmers
Name: Georgia Miller[36]

Key issues

Global agriculture and food systems are under acute stress

Industrial scale chemical-intensive agriculture has resulted in biodiversity loss, toxic pollution of soils and waterways, salinity, erosion, desertification and declining soil fertility (FAO 2007). Nearly a billion people face extreme food insecurity.

Empowering small scale farmers to meet their own food needs is essential

Around 75% of the world's hungry people live in rural areas in poor countries (FAO 2006). If rural communities can meet more of their own food needs via local production, they will be less vulnerable to global price and supply fluctuations. La Via Campesina has argued that: "Small-scale family farming is a protection against hunger" (La Via Campesina 2008). The four year International Assessment of Agricultural Science and Technology for Development emphasized that to redress rural poverty and hunger, small scale farmers must be empowered to meet their own food needs (IAASTD 2008).

Nanotechnology is likely to intensify economic pressures on small farmers

Nanotechnology proponents (IFRI 2008) and academics keen to promote the Millennium Development Goals (Salamanca-Buentello et al. 2005) have suggested that nanotechnology's use in agriculture will deliver environmental sustainability and eradicate hunger. Friends of the Earth Australia suggests that by entrenching dependence on industrialized, export-oriented agricultural systems and the chemical and technology 'treadmills' that underpin it, nanotechnology is more likely to intensify pressures on small farmers.

Nanotechnology has transformative potential – not just 'good' or 'bad'

Although our analysis is that on the whole nanotechnology is likely to intensify pressures on small farmers, we recognize that agricultural nanotechnologies do not present dichotomous 'advantages' and 'disadvantages'. In many instances the same technology poses advantages and disadvantages to different actors, as well as broader challenges. Agricultural nanotechnologies could also have profoundly transformative effects. They could radically alter the nature of farming systems, rural communities, agricultural biodiversity and food production (Scrinis and Lyons 2007).

High tech nano-agriculture aims for more uniform, more efficient, less labour intensive systems: this poses diverse social and economic challenges

The vision of many proponents of agricultural nanotechnologies is one of precise production: more uniform, more efficient, less labour intensive, more remotely managed, atomically 'improved' crops whose high productivity is made possible by entwined nano-surveillance and 'smart' farm management systems, nano-modified seeds and specialist interactive chemical treatments (USDA 2003). This could accelerate land consolidation, agribusiness

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[36] Friends of the Earth Australia

growth at the expense of small farms, increase monoculture production and result in further loss of agricultural biodiversity.

Agricultural nanotechnologies will have comparatively high capital costs, but deliver greater efficiencies in operation. This could deliver a near-term competitive advantage to larger or wealthy farmers who could afford them, while being inaccessible to smaller, poorer farmers. By underpinning the next wave of technological transformation of the global agriculture and food industry, nanotechnology appears likely to further expand the market share of major agrochemical and seed companies, food processors and food retailers to the detriment of small operators (ETC Group 2004; Scrinis and Lyons 2007).

Agricultural nanotechnologies pose significant intellectual property challenges. 'Smart' surveillance and nano-farm management systems could embed traditional farming knowledge in proprietary technologies to which access would require purchase. This could result in loss of traditional farming knowledge, entrenching reliance of farmers on technologies that they do not control and are unlikely to have the specialist knowledge or equipment to maintain. This will undermine the self-reliance of small farmers.

Remote or automated farm management systems may be vulnerable to technology malfunction, interference, or breakdown. It is conceivable that a given manufacturer or owner of 'software' could at some future point be unable to service agricultural nanotechnologies on which farm management comes to depend.

Each wave of technological innovation has created further efficiencies and consequent waves of job-shedding in agricultural industries (Hisano and Altoé 2008). At this early stage of nanotechnology's development there is no data specific to it. However we do know that the development of highly efficient, automated farm management systems is a key aim of nanotechnology proponents. Reducing on-farm labour is often touted as a positive. However further reduction in rural employment could promote increased rural-urban migration. The declining viability of small scale farms and falling jobs in the rural sector has already caused 'distress' migration of farmers to urban areas in many Southern countries, resulting in a rapid increase in urban poverty (FAO 2002).

Nanotechnology also poses health and environmental challenges

Combined nano-surveillance systems and 'smart' automated farm management could potentially reduce the need for on-farm inputs (eg fertilizers, pesticides, water) by targeting applications to more precisely identified needs. This could lead to water savings. However although such systems may reduce the quantity of agro-chemicals used, they entrench dependence on a chemical-intensive model of agriculture at a time when there is growing interest in agro-ecological and organic farming.

Proponents of nanotechnology also suggest that because nano-agrochemicals are formulated for increased potency, they will be used in smaller quantities, thereby delivering environmental savings (Joseph and Morrison 2006; USDA 2003). However, due to the increased potency of nano-agrochemicals, this may not reduce their toxicological burden. The Woodrow Wilson International Center for Scholars has suggested that the toxicological impact of 58,000 tonnes of manufactured nanomaterials might be the equivalent of 5 million or even 50 billion tonnes of conventional materials (Maynard 2006).

Nano-chemicals and nano-modified seeds may introduce novel environmental and health toxicity. There is preliminary evidence of serious health and environment risks associated with manufactured nanomaterials (RCEP 2008; SCENIHR 2009) and acknowledgement by leading researchers that the extent of uncertainty is such that reliable risk assessment systems do not yet exist (Hansen 2009; Oberdörster et al. 2007). The European Food Safety Authority (EFSA 2009) has stressed that scientists do not yet have the capacity to design a risk assessment process in which we can have confidence, and which is capable of guaranteeing safety:

"Although, case-by-case evaluation of specific ENMs [engineered nanomaterials] may be currently possible, the Scientific Committee wishes to emphasize that the risk assessment processes are still under development with respect to characterization and analysis of ENMs in food and feed, optimization of toxicity testing methods for ENMs and interpretation of the resulting data. Under these circumstances, any individual risk assessment is likely to be subject to a high degree of uncertainty. This situation will remain so until more data on and experience with testing of ENMs become available" (EFSA 2009, p2-39).

Leading nanotoxicologists have cautioned that validated nano-specific risk assessment methodologies may take many years to develop (Maynard et al. 2006). The need to adopt the precautionary principle to manage the serious but uncertain risks associated with nanotechnology has been recognized explicitly by governments from 5 continents. At the 2008 International Forum on Chemical Safety 71 governments, 12 international organizations and 39 NGOs recommended "applying the precautionary principle as one of the general principles of [nanotechnology] risk management" (IFCS, 2008).

The use of nanotechnology in agriculture is of particular concern as it involves the intentional release of agricultural pesticides, plant growth treatments and modified seeds into the environment. Very few studies have examined the ecological effects of nanomaterials and their behaviour in the environment remains poorly understood. For example it remains unknown whether or not nanomaterials will accumulate along the food chain (Boxhall et al. 2007). In its seminal report on nanotechnology, the United Kingdom's Royal Society and Royal Academy of Engineering recommended that the release of nanomaterials into the environment should be avoided as far as possible (Recommendation 4, RS/RAE 2004).

Potential solutions to address challenges identified

Firstly, given the serious nature of the crisis gripping agriculture, we must not assume that certain technologies offer unproblematic solutions. We must clarify the goals of agricultural policy and development before we can evaluate the extent to which nanotechnology or other technologies can offer solutions, or to which they may simply exacerbate existing problems. Friends of the Earth Australia (FOEA) suggests that the key goals of agricultural policy should be to reduce hunger, to strengthen the self-reliance of small farmers, to improve the ecological sustainability of food production, to maintain agricultural biodiversity and to prepare for a deepening of existing stresses associated with climate change and population growth.

Secondly, we must evaluate the extent to which technological and non-technological options are able to contribute to the goals of agriculture and development. We suggest that nanotechnology, along with other technology and non-technology agricultural options, should be evaluated in relation to its likely contribution to meet the needs of small farmers while

bolstering, rather than diminishing, their own sufficiency and capacity for self-reliance. In our assessment, while it offers apparent advantages in some aspects, nanotechnology is likely to add to the pressures faced by small farmers, thereby posing a net cost.

It is always worthwhile to query to what extent negative aspects can be overcome through policy initiatives. However FOEA is concerned that there is no ready solution to nanotechnology's probable intensification of pressures on small farmers as the problem exists at a number of levels:

Economic/commercial pressures

Intellectual property: Nanotechnology research is expensive and to a large extent, public and private sector sponsors will be looking to recoup research outlays through product commercialization. A potential solution is to support substantive intellectual property reform that would result in delivery and future maintenance of free agricultural nanotechnologies. However this appears practically improbable, especially in the long term. Further, short-term 'honeymoon' deals (eg where agricultural nanotechnologies may be offered free or at a reduced cost for some initial period of time) would simply delay the problem, while promoting uptake of and reliance on nanotechnologies now

Entrenched reliance of farmers on corporate technologies: Due to the elite nature of nanotechnology research, its utilization as a 'black box' technology is inescapable. To the extent that nanotechnology 'smart' farm management systems, 'smart' agrochemicals and surveillance systems did replace on-farm labour, these would also commodify existing farm management knowledge and embed it in these new proprietary systems.

Systemic tendencies that increase commercial pressures on small farmers: It is likely that nanotechnology would increase scales of production, uniformity of produce, growth of monoculture crops, consolidation of farms into larger units and more production for export markets. It is unlikely that nanotechnology would result in greater agricultural biodiversity, greater diversity of small farms, greater empowerment of small farmers or more production for local markets. There is no solution to this – nanotechnology has inherent tendencies to centralization.

Social pressures:

Social/economic disadvantage: Many social pressures overlap with the economic pressures identified above. This is especially acute in relation to the potential loss of rural/on farm employment, the potential further consolidation of small farms into larger farms and the likely social upheaval that would result as rural migration intensified. The potential commodification/loss of farming knowledge is also a serious social and cultural issue. As discussed, there are no ready solutions here.

Right to choose: Measures can and should be implemented to enable small farmers and farming representative bodies to take part in decision making about nanotechnology policy, research funding allocation and government support for industry development. This requires not only labelling, education and information to enable individual farmers to make decisions about their own use of nanotechnologies, but also explicit recognition of the right of local farmers and faming communities to participate in decision making about agricultural policies

that affect them, including the adoption or rejection of elite technologies, and the extent to which public research funding should be invested in this research and industry support

Government policy – ensuring public interest management of nanotechnology

<u>Assessing opportunity costs of nanotechnology investment</u>: FOEA is concerned about the opportunity cost of investing in nanotechnology research, development and commercialization in preference to more sustainable and localized farming models, or in social and economic initiatives to better support small-scale farmers. A solution is for governments to conduct an assessment of the capacity of nanotechnology to meet key social and environmental objectives, compared to other technology and non-technology options. This should inform the allocation of public funding for research and industry support

<u>Prioritizing public interest science</u>: public funding should be targeted to research and development that has a demonstrable public interest benefit, where the needs of small farmers are prioritized over the competitiveness of agribusiness at large

<u>Environment and health impacts associated with nanotechnology in agriculture</u>:
Some environmental pressures associated with agricultural nanotechnologies do not have a ready solution (eg probable acceleration of loss of agricultural biodiversity associated with increasing tendencies to larger farms, more uniform produce)
The novel environment and health risks associated with the use of nano-formulated agrochemicals, seeds and other agricultural products should be regulated according to the precautionary principle. Nano-forms of bulk chemicals should be treated as new chemicals and subject to new, nano-specific safety assessment. The onus should be on the product proponent to demonstrate safety

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Title: Applications of Nanotechnology in Agrochemical Formulation：Perspectives, Challenges and Strategies

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Introduction

Nanotechnology offers a new way for transforming the formulation of agrochemicals, such as bioactive compounds, fertilizers, growth regulators, herbicides, and pesticides, etc. Nanostructured formulation could release their active ingredients in responding to environmental triggers and biological demands more precisely through targeted delivery or controlled release mechanisms. Such nanobased agrochemical products hold great potential to benefit the environment in terms of reducing overall chemical usage that may cause pollution in the water system and contamination in crops and food products. Therefore, nanotechnology has become a new impetus for overall sustainable agriculture, especially in developing countries. Here our focus is placed on the challenges and the overcoming strategies regarding development of nanopesticides and nanofertilizers.

The R&D Status and Prospects of Nanopesticide Formulation

The loss and decomposition rate of active ingredients in conventional pesticides during the application process is typically up to 90%. The actual utilization of biological targets is only less than $1/10^4$. Using nanoscale and nanostructured materials as delivery carriers and vector systems might bring about beneficial changes in properties and behaviour of pesticide formulation, such as solubility, dispersion, stability, and targeting delivery efficiency, and controlled release of active ingredients. Furthermore, it might also not only significantly improve the bioavailability and the duration of drug efficacy, but also reduce the residual contamination of food and environment. There are many advantages for nanopesticides as summarized in Table 1.

Table 1. Opportunities for Nanotechnology in Transforming Pesticide Formulation

Desirable Properties	*Examples of Nanopesticieds-Enabled Technologies*
Targeted delivery and controlled release	Controlled release speed of active ingredients to maintain the least effective concentration for killing pests and pathogens in environmental media and biosystems continuously and dynamically
Solubility and dispersion for insoluble ingredients	Aqueous colloid and nanosuspension of pesticides substitute EC Products aimed for avoiding the pollution of organic solvents
Chemical stability	Nanoencapsulated biopesticides, such as antibiotics, growth stimulants and bioactive agents, might display excellent properties in stability, bioavailability and persistence of the bioactive chemicals by restricting photodegradation
High bioavailability	Reduced use of pesticides in crop protection
Longer duration of	Reduced application of pesticide and related labour cost

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persistence	
Controlled release and delivery modes	A formulated high-efficacy delivery and controlled release system for pesticide encapsulated in nanocapsules and mesoporous nanoparticles
Lower toxic to non-target wildlife	Protected biodiversity in agricultural ecosystem
Lower residual pollution	Reduced food residues and non-point source pollution due to the minimum pesticide loss

Currently, most research on nanopesticides in China is primarily focused on the improvement of environment friendly properties to overcome environmental and food safety problems due to the application of pesticides in crops production. A multi-disciplinary research team led by Chinese Academy of Agricultural Sciences is investigating the targeting delivery and controlled release of agricultural bio-drugs, including bio-pesticides, veterinary medicines and vaccines. This research is supported by the National High-Tech R&D Program, (863 Program), Grant No. 2006AA10A203, and Grant No. 2007AA021808. Some significant progress has been achieved in the area of nanoencupsulation and nanostructed carriers as controlled release and delivery systems for agro-antibiotics, such as avermectin, ivermectin, and validamycin, etc. Such achievements might facilitate the larger scale uses of bio-pesticides in crop production. The nanoemulsion of some fat-soluble pesticides has been developed successfully. Mesoporous particles, such as nanoclay, activated carbon and porous hollow silica, were also verified to be suitable for the controlled release and delivery carrier systems for the water-soluble and fat-dispersible pesticides that have a high drug-loading capacity and multistage release pattern. However, there are some technical obstacles that need to be addressed in the near future (Table 2).

Table 2. Priority Issues in R&D of Nanopesticides

Technical Obstacles	Priority Issues of Nanopesticieds-Enabled Technologies
Delivery carrier systems formulated by mesoporous material or molecular sieve	To control the release speed of active ingredients in response to environmental and biological triggers and reduce food residues and environmental pollution caused by loss of pesticide compounds
Nanoencapsulation in the form of nanocapsules, micelles, liposomes	To stabilize the chemical properties and bioactivity of pesticides by using nanoencapsulation to protect active ingredients sensitive to light, such as bio-based compounds, from photo-degradation
Targeting compound modification	To increase the targeting delivery efficiency through improving behaviors of wetting, spreading and absorbing of drug droplets on surface of leaves, and penetration and uptake of active compounds into the infected organs, insects or pathogens
Nanosized processing	To render higher solubility and dispersion for insoluble or fat-dispersible compounds in aqueous solution
Inclusion complexes	To control release and protect drug molecules by absorbing pesticides with nanostructured polymers or mesoporous materials, such as hollow fiber, porous silica and activated carbon
Granulation coated with nanostructured-polymers	To create slow/controlled release formulation of insecticides and fungicides to control soil infection diseases and soil pests
Nanoemulsion	To increase solubility and dispersion for fat-soluble drugs in aqueous solution by self-emulsifying delivery system
EC alternative products	To develop an environment friendly formulation without toxic

with aqueous colloid dispersion system	organic solvents for fat-soluble compounds, which is easily dissolved and dispersed in aqueous solution

Based on the current research progress on nanopesticides in China, it is our expectation that the following R&D objectives will be realized in the next 5-10 years.

- Slow/controlled release formulation of insecticides and fungicides might be widely used for the control of soil infection diseases and soil pests so as to reduce chemical residues and pollutants in soil and foods caused by leaching and leaking of toxic ingredients in pesticides.
- Aqueous colloid dispersion and nanosuspension of pesticides would gradually substitute EC products to avoid the pollution of organic solvents.
- Nanoencapsulated bio-pesticides, such as antibiotics, growth stimulants and bioactive agents will gradually replace their conventional equivalents because of their excellent properties in stability, bioavailability and persistence of the bioactive chemicals.

The R&D Status and Prospects of Nanofertilizer Formulation

The yield-increasing effect of fertilizers is subject to the *law of diminishing marginal returns. With the increase in the amount of fertilizer per unit area, its input-output efficiency and nutrient absorbing rate will reduce continually. On the contrary, Soil nutrients lost will increasingly exacerbate water body and non-point source pollution. Currently, the average utilization rate of chemical fertilizer in China is typically less than* 30%. In other words, more than 70% fertilizer nutrients are lost through processes in the soil such as leaching, leaking, bio-transformation and soil fixation. Thus, the development of precisely controlled release fertilizers based on nanotechnology has become critically important for promoting the development of environment friendly and sustainable agriculture. Application of nanotechnology has demonstrated great prospects in the breakthrough of technical bottlenecks of slow/controlled release fertilizer using Nanoscale or nanostructured materials as fertilizer carriers or controlled-release vectors for constructing of so-called "smart fertilizer." The development and application of nanofertilizers will demonstrate some advantages over their conventional counterparts such as: (1) increased efficiency and quality of nutrient supply with a higher uptake rate; (2) releasing fertilizer nutrients at a dynamically controlled rate throughout the season so that plants are able to take up most of the fertilizers without loss by leaching; (3) substantial reduction in pollution of soil, water reservoirs and food products; (4) mitigation of soil compaction and quality deterioration; (5) reduction of plant toxicity and stress from high local concentrations of salts in the soil; (6) reduction of fertilization costs by reduced fertilizer dose and application frequency ; (7) increased crop production by the improved nutrient status; and (8) improved storage and handling properties of fertilizer materials . The R&D advances on nanostructured formulation of fertilizers are summarized in Table 3.

Table 3. Recent R&D Objective and Progress of Nanofertilizers

Desirable Properties	*Examples of Nanofertilizers-Enabled Technologies*
Controlled release formulation	So-called smart fertilizers might become reality through transformed formulation of conventional products using nanotechnology. The nanostructured formulation might permit fertilizer to intelligently control the release speed of nutrients to match the uptake pattern of crop
Solubility and dispersion for mineral micronutrients	Nanosized formulation of mineral micronutrients may improve solubility and dispersion of insoluble nutrients in soil, reduce soil absorption and fixation and increase the bio-availability
Nutrient uptake efficiency	Nanostructured formulation might increase fertilizer efficiency

	and uptake ratio of the soil nutrients in crop production, and save fertilizer resource
Controlled release modes	Both release rate and release pattern of nutrients for water-soluble fertilizers might be precisely controlled through encapsulation in envelope forms of semi-permeable membranes coated by resin-polymer, waxes and sulphur
Effective duration of nutrient release	Nanostructured formulation can extend effective duration of nutrient supply of fertilizers into soil
Loss rate of fertilizer nutrients	Nanostructured formulation can reduce loss rate of fertilizer nutrients into soil by leaching and/or leaking

In China, the development of nanobased slow or controlled-release fertilizers has been actively implemented since the beginning of this century and supported by the National High-Tech R&D Program. Significant progress has been made, especially on film-coating urea and granular compound fertilizers. Some nanobased agrochemicals have been commercialized. The solubility and dispersion of insoluble mineral micronutrients and phosphate fertilizers have been significantly improved by nanosized or nanostructured processing. However, there are still some major technical obstacles and priority issues that need to be addressed and overcome in the near future (Table 4).

Table 4. Key Technical Obstacles and Priority Issues in R&D of Nanofertilizers

Technical Obstacles	*Priority Issues of Nanopesticieds-Enabled Technologies*
Film coated granulation with nanopolymers	To create granular compound fertilizers with smart controlled release modes in order to reduce fertilizer loss occurring on the process of leaching, bio-degradation, and migration of fertilizer nutrients in soil, and inhibit non-point source pollution and water body eutrophication
Nanosized preparation of insoluble nutrients	To improve solubility and dispersion of mineral micronutrients and phosphate fertilizers aimed to increase absorption efficiency by inhibiting soil absorption and re-mineralization, and immobility
Compound absorption with mesoporous materials, such as nanoclay and porous minerals	To develop multi-compound fertilizer with property of precisely controlled release in order to improve fertilizer nutrients efficiency and synergistic effect
Sulphur or paraffin coated Encapsulation	To develop environment-friendly and controlled release formulation for soluble nitrogen fertilizer encapsulated or coated by sulphur or paraffin wax, such as sulfur coated urea

With the current development, by the next decade, nanostructured formulation of controlled release fertilizers will become a mature technology that will enable wider application in large-scale crop production for developing countries. The applications may primarily include following aspects: (1) promotion of environment friendly and green crop production, especially the production of paddy and horticultural crops, inhibiting soil non-point pollution and water body utrophication; (2) increase of *input-output efficiency in crop production through the improvement of* fertilizer efficiency, and promote development of sustainable agriculture; (3) overcoming of resource shortage of mineral micronutrients and phosphate fertilizers by the application of higher efficiency nanostructured products.

Potential Risks and Barriers in the Development of Nanoagrochemicals

Nanoagrochemicals have a great potential to have their *input-output efficiency enhanced*, giving ecological and environmental benefits. However, these advantages might be offset by some potential risks of human health and ecological disasters. The general concern is that some nanoparticles or nanostructured materials may flow into the environmental systems and food from nanoagrochemicals or agronanochemicals may be toxic, which may become a new class of pollutant resources that threaten human health and ecosystem balance. Therefore, more research is needed on safety and risk assessments of nanoagrochemicals. The results on studies of toxicology and safety evaluation of nanobased medicines may be referred to agrochemicals, as they used some similar technical lines and ideas. Also, in the development and production of nanoagrochemicals, nanostuctured materials with larger size particles might be more safe and effective than solid nanoparticle materials used for delivery carrier and control release media in transforming formulation of fertilizers and pesticides.

Although nanoagrochemicals dominated by fertilizers and pesticides worldwide appeared to havee good prospects in promoting environment friendly and sustainable agriculture, the high cost of nanoagrochemicals, which is generally 3 to 4 times more expensive than the conventional products, forms a huge barrier for their large scale application in crop production for developing countries. However, as the expansion of production scale and application scope happens, market price will be reduced sharply. Increased cost by slightly higher unit price of the product could be offset by saving per unit area, as their level of efficiency is twice as high as conventional equivalents. Henceforth, the application of nanoagrochemicals in crop production should be treated as a novel, innovative, strategic high-technology or focused on ecological and environmental benefits to implement financial support or subsidies. In general, the use of nanoagrochemicals starts to evolve as a promising direction offering an excellent means to improve management of fertilization and crop protection by reducing significantly environmental threats while maintaining high crop yields and good quality.

Strategies for Promoting Applications of Nanoagrochemicals in Developing Countries

In order to facilitate applications of nanoagrochemical technologies in developing countries, the following strategies and management policies should be implemented:

1. **Strengthen R&D activities and innovation platform:** State/provincial or central government agencies should have clear R&D priorities suitable for the state/province or the region, and actively engage in universities and research institutions in the debate of R&D priorities, then strategically increase priority R&D budget for multi-disciplinary collaborative research activities, therefore to strengthen research infrastructure and platform establishment.
2. **Improve extension system and support policy:** An integrated extension system should be in place in order to promote the integration of R&D activities with industry and economic development, strengthen the management of the processes of technical extension and products production. Support policies including financial support measures should be established and actively enforced.
3. **Enhance product quality assurance and supervision and market management:** This is a policy issue. It is absolutely necessary to establish specific product standards, the validation and registration rules for nanoagrochemicals should be actively enforced.

Concluding remarks

Clearly, nanofertilizers and nanopesticides have many advantages over their conventional equivalents such as high efficiency, environment friendliness, high-targeting delivery and smart controlled release. Due to their technological advancement, large scale applications of nanofertilizers and nanopesticides in crop production have just become possible. As a most promising and attractive field of nanotechnology application in agriculture, these novel agrochemical products will provide multiple benefits such as reduced use of chemicals and subsequently reduced water pollution and food product residual contamination, efficient use of agricultural resources, increased soil and environmental qualities. As a novel high-tech for agriculture, nanotechnology will no doubt help ensure food security, development of environment friendly and sustainable agriculture in developing countries and regions. Central and/or state/provincial government agencies should and must have clear R&D priorities and governing policies in place, strategically invest in such high tech areas to strengthen the construction of research infrastructure and platform and product development, and applications of such nanotechnology products through integrated extension system.

Annex III
Round Table 3 background paper and related mini papers

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Round table 3
Background paper
Nanotechnologies: regulatory framework
General insight on regulatory framework and nanotechnologies

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1 Introduction

The application of nanotechnology in the food and feed industry offers many potential benefits for both consumers and society. Nanotechnologies enable the manipulation of matter at the nanoscale level that results in new properties and characteristics that can be beneficially exploited in food production and processing. Some of the potential benefits for consumers include foods with lower fat, salt or sugar levels that taste similar to conventional foods; improved packaging material that keeps food fresher for longer or tells consumers if the food inside is spoiled; and innovative food contact surfaces and materials that allow for improved food hygiene standards during food manufacture. There is also the potential to increase bioavailability of food additives and ingredients through the application of nanotechnology and to enhance the uptake of micronutrients in human and animal nutrition.

Nanotechnologies may also present new risks as a result of their novel properties. There are a wide variety of nanomaterials and while many of these may well prove to be harmless, others may present a risk to human health. Traditional food manufacturing processes result in the creation of nano-sized particles in emulsions and biological matrices that have been always present in foods. Such natural nanoscale substances have been consumed for many years without harmful effects being reported, for instance milk contains micelles ranging from 50 to 500 nm in diameter. On the other hand our current understanding of how engineered nanomaterials that are deliberately introduced into foods behave in the human body is not sufficiently advanced to predict with certainty impacts on human health. We have limited data on the functionality and toxicological impact of such nanomaterials, particularly in areas relating to the risks posed by ingested nanomaterials. Such information is required in order to ensure that regulatory agencies can effectively assess the safety of products before they are allowed onto the market. In order to properly develop, modify or in particular to implement legislation, our scientific knowledge base needs to be expanded and improved.

The introduction of nanotechnology in the food sector and its acceptance by consumers will depend to a large extent on the confidence people have in the effectiveness of regulatory systems in place to ensure that consumers are protected against any potential risks. The application and use of nanotechnology must comply with a high level of protection of public health and consumer safety, as well as protection of the environment. The regulatory challenge is therefore to ensure that society can benefit from novel applications of nanotechnology, whilst a high level of protection of health, safety and the environment is maintained. A reliable and stable regulatory framework is essential for enabling the food industry to fully exploit the advances and potential of nanotechnologies.

2 Food regulations

There are few areas in the nanotechnology debate that are under more scrutiny than regulatory considerations. It is an area that requires attention in the short-term as uncertainty over regulations for the use of nanotechnologies and nanomaterials in the food sector may stifle research and overall development. Key questions relate to whether current

food regulations are sufficiently robust to be applied to nanotechnologies and whether risks can be dealt with under current legislative frameworks. At present there are no "nano-specific" food regulations in place but specific regulations are under development in various countries and regions. Global harmonized regulatory frameworks have not been developed but issues are being discussed at international level within the Organisation for Economic Cooperation and Development (OECD), the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO).

The broad areas of the food processing and manufacturing sectors with potential for the application of nanotechnology include food additives and ingredients, food packaging materials, food contact materials and novel delivery systems. The focus of regulation should be on engineered nanomaterials that are deliberately introduced into the food chain. Such engineered nanomaterials range from food contact material, ingredients and additives, to fertilizers and pesticides that are used in the food and feed area. Traditional nanoscale materials that occur naturally in food matrices should also be the focus of regulations if they have been deliberately used or engineered to have nanoscale properties or used in the manufacture of bioactive compounds.

A major challenge in the development of a regulatory framework for nanotechnology and nanomaterials is the absence of a common definition; agreement is required on what is being regulated if certain products or processes are not to fall between regulatory gaps. For the food industry to comply with regulations that govern nanotechnology there must be a clear definition of what they have to comply with so that they do not fall foul of compliance. In the interests of consumer protection a definition of nanomaterials should be added to food legislation to ensure that all nanoscale materials that interact differently with the body as a result of their small size are assessed for risk before they are allowed on to the market.

There are strong arguments that in the interest of protecting consumers' health food legislation should ensure that all engineered nanomaterials used in the food sector undergo a safety assessment before they are allowed on to the market. Engineered nanomaterials are specifically designed and manufactured with the intention of being incorporated into food to fulfil a particular function. In this regard a regulatory definition of nanotechnology is required that is based on functionality of the engineered nanomaterial. The functionality is related to the novel size, shape, surface area and physico-chemical properties of the nanomaterial.

3 Current regulatory frameworks

A recurring question regarding regulations targeting the safe use of nanomaterials and nanotechnology in food and feed relates to the adequacy of current regulations to cover potential risks to consumer health. Food regulations already exist for food additives, micronutrients and essential elements, residues of pesticides and veterinary drugs, and for food packaging and food contact materials. Current regulations cover conventional foods where risks are assessed on a "macro-scale" for chemical ingredients, other components and contact materials prior to placing on the market. Additionally current regulations cover monitoring and surveillance programmes for residues and contaminants in the food chain

which are based on established laboratory sampling and analytical methods. Many of our existing regulations were not designed with nanomaterials in mind so it is not surprising that provisions may not afford adequate consumer protection.

Current regulations cannot be directly applied to "nano-scale" ingredients or components in foods and modifications will be required to capture new developments in food processing and manufacture. Difficulties arise in characterizing the properties of nanoparticles when attempting to carry out an estimation of consumer exposure. Difficulties also arise as analytical techniques to measure concentrations of nanoparticles in foods are not fully developed. Also limit values for nanoparticles cannot be expressed in weight or volume measures as is the case for conventional chemicals because of the altered functional properties associated with the size, shape, surface area and surface chemistry.

Different countries and regions are adopting different approaches. For instance in the European Union the general food law prohibits the placing on the market of unsafe foods were the responsibility is on the food business operator to ensure the safety of food products. New food ingredients and agents used in food and feed manufacture must be subject to a pre-market safety assessment. At European level regulations are evolving to include the utilization of nanotechnology in foods, for instance a new regulatory requirement specifies that approved food additives that have been subjected to a size reduction to the nanoscale should be subjected to a new risk assessment before being placed on the market. In the United States any new foods or food ingredients are subject to pre-market safety assessment regardless of how they are manufactured. In Japan there are no specific requirements for nanotechnology in food regulations, however, current regulations ensure that only safe foods are placed on the market.

4 Research needs to support the regulatory base

There is a need to improve current scientific knowledge base to support the regulatory base. Current uncertainties for risk assessment are associated with the applications of nanotechnology in food and feed due to the limited information on methods to characterize, detect and measure nanomaterials and nanoparticles. Key areas where research is required are in the areas of the development and validation of reliable methods to measure relevant properties, such as size, shape, surface area and surface chemistry, particle size distribution, physiochemical and biological parameters in food different matrices. There is also a need to develop and validate methods to detect the effects of nanomaterials on human health to include acute and chronic toxicity, bioavailability, toxicokinetics, and exposure assessment. Similar research and development needs exist relating to persistence, bioaccumulation and degradation of nanomaterials in the environment and the development of regulations. It is important for governments and international agencies to cooperate and collaborate to ensure that knowledge gaps in research related to the health and safety risks of nanomaterials are filled quickly without duplication of effort.

5 Knowledge gaps impacting on development of regulatory frameworks

As applications of nanotechnologies and nanomaterials develop and become increasingly dissimilar to conventional technologies and materials, gaps in the current regulatory frame work will become more pronounced. There are currently many areas of uncertainty surrounding the use of nanotechnology in the food and agriculture sectors that impact on the development of regulatory frameworks. These relate to a regulatory definition that should refer to the nanoscale with dimensions up to 1000 nm and to product functionality that defines how a substance interacts in biological systems.

When approved food additives and ingredients are reformulated at the nanoscale to confer new functional properties, such products should be subjected to a new risk assessment. Improved bioavailability of food supplements such as minerals and vitamins manufactured at the nanoscale may lead to redefining such regulatory concepts as acceptable daily intakes (ADI) or recommended daily intakes (RDI) in order to prevent risks of overdosing. The definitions of purity criteria will require information on the size and form of a substance.

With regard to regulations covering food contact materials, expressing regulatory migration levels in mass per mass or volume will not take into account the possibility of changing toxicity profiles with increased surface areas and smaller size. Regarding nanoscale food contaminants there may be a need to revalidate human health limits such as provisional tolerable weekly intakes (pTWI) or tolerable daily intakes (TDI) due to possible increased toxicity of nano-sized particle contaminants. Similarly additional safety testing or new approvals may be required where nano-particles are included in pesticides or utilized in veterinary medicines. The absence of routine analytical methods to detect nanoparticles in foods will hinder the application of monitoring and surveillance programmes that underpin the application of food regulations.

Where the risks posed by a nanomaterial cannot be fully determined, products should be denied regulatory approval until further information is available.

Round Table 3 mini papers

Title: Partnerships and collaborations in Research and Development and regulatory issues
Name: Thembela Hillie[38]

Introduction

It is well accepted that a significant change in the quality of life, from the more successful emerging societies to the poorest, can only happen through knowledge, technology and innovation. Nanotechnologies have promised numerous benefits across the board. The proponents of nanotechnology are confident that it will deliver the Millennium Developmental Goals (MDGs) to solve the problems that still confront the developing countries. They also promise to provide alternative technological solutions that will be successful in mitigating the effects of climate change. Contrary to the promises are the realities that are encountered in any development and transfer of any technology and these are also pronounced in nanotechnologies. They include the cost, infrastructure, technical capacity for research and development and regulatory issues. Although these are expected and are easily addressed in the developed world, they might prove to be impediments in the developing world. This mini paper seeks to address these issues and suggest ways to overcome them.

Key issues to be discussed

Nanotechnology provides opportunities for everyone to be involved in addressing their own priorities. This is so because nanotechnology has different levels of sophistication which are related to the complexity of integration and control of fundamental properties. There are four perceived generations of nanotechnology development which are passive nanostructures, active nanostructures, systems of nanostructures and molecular nanosystems and they have different timeframes to be realized. Developing countries are at different levels of scientific progress and capacity in terms of expertise and infrastructure. Some of the developing countries are already engaged in nanotechnology with some coordinated efforts to consolidate research pockets, whilst some have national nanotechnology strategies [1] to inform these activities. Although the problems are different, they are also similar presenting prospects for collaborations.

Cost issues

It is believed that it is incorrect to assume that nanotech is too difficult or too expensive to be implemented in developing countries and it may be a critical tool for research and development to offer important benefits. The costs associated to carrying out nanoscale science research is not a significant issue at the passive stage, as most of the research is still under traditional science disciplines with emphasis on the novel properties at nanoscale. This will be different with the progression to more advanced research. The critical aspect in relation to research is the characterization of nanomaterials which requires sophisticated microscopy and in some cases instrumentation in well established facilities.

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Infrastructures

Successful nanotechnology research and development also depends strongly on the supportive infrastructure in place. Characterization remains the most expensive aspect, especially in nanotechnology research and can be critical in widening the gap in nanoscience between the developing and developed countries. Promoting cooperation among facilities and providing access to the less developed countries and disseminating information on advanced user facilities worldwide could assist in this regard.

Technical capacity for R&D on nanoscience and nanotechnology

Local capacity in nanoscale science and nanotechnology is crucial for the successful development and implementation of nanotechnology. It is also essential for the adoption and adaptation of the technologies which are not developed locally. Capacity building can be facilitated through research institutions of the respective countries by developing common research projects which will promote the movement of students and scientists among these institutions. These exchange visits should be budgeted for as part of the partnership.

Regulatory issues

The issues of governance and regulation have been a subject of concern globally. There are various platforms that have been created to provide a uniform approach to these issues. The OECD dialogues in responsible nanotechnology research, the International Risk Governance Council and the International Organization for Standardization committees in nanotechnologies are some of these platforms. Participation in them is critical and it should be an inclusive exercise to promote responsible nanotechnology research across the board

Challenges identified

Local Capacity

Building local capacity of expertise to adopt and adapt some of the developed nanotechnologies and tailor make them for the local needs. This is vital for sustainable development and the transfer of nanotechnologies in developing countries.

Awareness

There is lack of awareness in society at large, including business, about both the risks and opportunities that nanotechnology can offer. There is a need for public engagement to promote broader stakeholder participation that will inform local priorities.

Policy frameworks

For an effective sustainable development of nanotechnology, governments should drive the process and commit funds and strategic support to the initiative. This is still lacking in

developing countries and poses a challenge to the existing fragmented research pockets to consolidate.

Strategies to overcome the challenges

What has been done so far and what is missing

There are lot of active research pockets in developing countries and these are tailored to their priorities. A lot of country to country bilateral, be it North-South or South-South, have nanotechnology as an area of interest. Access to research infrastructure is facilitated and exchange visits are utilized to build human capital. Missing in some countries are national strategies and policies to provide direction for all the stakeholders. The council of emerging technologies of the World Economic Forum has proposed an institute that would address three challenges in particular, namely (1) working effectively across traditional boundaries (including scientific, organizational and national boundaries); (2) effective technology development and technology transfer; (3) and predicting, assessing and avoiding adverse consequences of emerging technologies. It also aims to engage the society for its input to inform the priority areas.

Mechanisms for knowledge transfer on Nanotechnologies

Nanoschools

Nano schools to train young researchers, theme meetings in identified areas of mutual interests and specialized workshops in the area of nano research can be organized as part of Human Capacity development programs. These schools can be on a specific area of interest i.e. flagship projects, and the host countries can rotate to give maximum benefit to the local students.

Exchange visits

In addition, exchange visits of scientists outside the scope of flagship projects and participation in relevant conferences/meetings organized by the participating countries could be supported under the partnership. This would eventually help to explore new areas of collaboration and to develop new flagship projects.

Virtual institutions

The organization of scientific research is undergoing a fundamental transformation with the emergence and growth of global science networks on the rise. The shift from big science to global networks creates unprecedented opportunities for developing countries to tap science's potential. Rather than squander resources in vain efforts to mimic the scientific establishments of the twentieth century, developing country governments can leverage networks by creating incentives for top-notch scientists to focus on research that addresses their concerns and by finding ways to tie knowledge to local problem solving [2].

Partnerships and Collaborations

Partnerships and collaborations based on a principle of equality and mutual benefits provide unique opportunities to promote transfer of knowledge and skills. They can help solve common problems with a concerted effort and stimulate the economies by exposing companies from the respective countries to different market demands and in some cases supporting risk through government financial support. Each partnership will be informed by a particular strategic objective and a country should be involved in a combination of these to benefit the broader stakeholder. Some of the examples of partnerships and their goals involving the developing countries are listed below:

South-South IBSA

IBSA is a trilateral, developmental initiative between India, Brazil and South Africa to promote South- South co-operation and exchange. The IBSA- Nanotechnology initiative is sponsored by the Republic of India-Department of Science and Technology, Federative Republic of Brazil-Ministry of Science and Technology and Republic of South Africa-Department of Science and Technology. India is recognized as leading the IBSA nanotechnology initiative. Advanced Materials, Energy, Health and Water are identified as the priority subject areas for this collaboration. Human resource development is also considered as a thrust area for the initiative [3].

Regional- Asian Nano Forum

Asian countries are at different levels of development and are assisting each other in developing nanotechnology for regional benefits. The Asian Nano Forum (ANF) is a network organization founded in 2004 to promote excellence in research, development and the economic uptake of nanotechnology within the Asian region [4]. The ANF seeks to benefit its member economies educationally, socially, environmentally and economically by fostering collaboration and acting as a focus for regional and global nanotechnology issues. The network is supported by 15 economies in the Asia Pacific region and the Middle East and has actively supported member economies with their national initiatives and events.

North-South ICS-UNIDO

The International Centre for Science and High Technology (ICS) seeks to promote excellence in science, catalyse collaborations between North-South and South-South, building human capabilities, and, specifically in the case of ICS, drive technological transfer to promote economical progress. Although nanotechnology is in its infancy, ICS realized that it was time to explore its implementation in developing countries to avoid another gap, similar to the digital and biotechnological gaps, between industrialized countries and developing countries.

There are other networks that are available, such as the Global Nanotechnology Network (GNN) [5] which is an international network of nanotechnology stakeholders dedicated to:

1. Facilitating an effective exchange of scientific, technical and educational information
2. Enhancing access to critical nano-related resources
3. Promoting global collaborations in nanotechnology research and education.

Some of the general benefits that the collaborations in R&D can provide are:

- The Expansion of scientist networks and the exposure of their work
- Access to critical infrastructure for research
- International experience for students
- Impetus to pursue new research areas
- Local expertise for adoption and adaptation of technologies

Importance of adequate policy to promote and support nanotechnologies development

The commitment by governments to formulate policies around nanotechnology provides direction and facilitates a required environment for a broader stakeholder involvement. It also provides the impetus to the private sector involvement and can rally other players such as research institutions behind the national objectives.

Conclusion

Nanotechnology research and development can also thrive in developing countries only if partnerships and collaborations can be established for mutual benefits and provide adequate access to facilities, which can be research facilities and commercial facilities of different size and scope.
There should be a resolve by governments at policy level to support the nanotechnology initiatives and commit funding as nanotechnologies have a potential to solve especially the needs of the poor.
Governance and regulation in nanotechnology have global consequences and only if inclusivity in participation in the existing platforms is promoted will the benefits for the developing countries be guaranteed.

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4. http://www.asia-anf.org/ANFNetwork.php
5. http://www.globalnanotechnologynetwork.org

Title: Concepts of Nanotoxicology
Name: Günter Oberdörster[39]

Introduction

Increases in nanotechnological applications for industrial, consumer and medical uses promise many benefits, yet at the same time they have generated serious concerns about potential health and environmental risks from exposure to engineered nanoscale materials (Fig.1). Such concerns stimulated research in the emerging field of nanotoxicology, resulting in a steadily increasing number of publications suggesting that engineered nanomaterials because of their specific physico-chemical properties can induce significant toxic responses. Although most of the nanotoxicological studies were performed using unrealistic exposure conditions, they have led to a widespread perception that generically all nanomaterials pose a significant health risk. Such perception is in great part based on exaggerated reporting in the popular press, resulting in a "Nanotoxicity-Hype Correlation (Fig.2). Knowledge about potential human and environmental exposure combined with dose-response toxicity information will be necessary to determine real or perceived risks of nanomaterials following inhalation, oral or dermal routes of exposure. Because the respiratory tract is the major portal of entry for airborne nanoparticles, this exposure route can be used as an example to discuss some key concepts of nanotoxicology, including the significance of dose, dose rate, dosemetric, and biokinetics. These include the importance of characterizing critical physico-chemical properties of nanoparticles, specifically surface properties that influence their biological/toxicological properties, cell-interactions and biokinetics. Misconceptions need to be corrected, such as the propensity of nanoparticles to translocate with high efficiency across barriers, or that the identification of a hazard based on unrealistic and unjustifiable high dose studies represents a useful basis for risk assessment. On the other hand, study results based on improbable high doses, *in vitro* as well as *in vivo*, may be viewed as proof-of-principle studies to be validated by appropriately designed follow-up studies using justifiable exposures. Under such realistic conditions, many engineered nanoparticles are unlikely to induce adverse effects, although still largely unknown are effects of chronic, low level exposures. Without being able to perform an appropriate risk assessment for a specific nanomaterial, due to the lack of hard data, it is prudent to prevent exposures by precautionary measures/regulations.
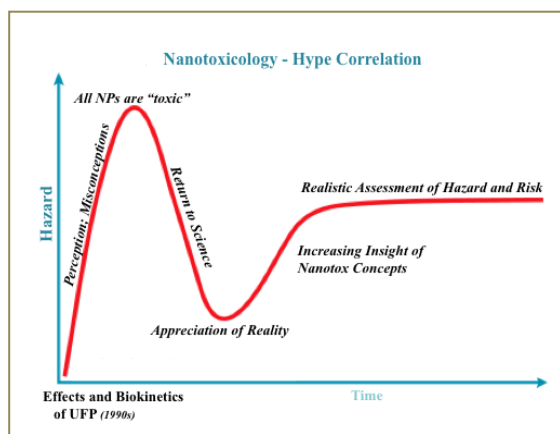

Figure 2

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Key Concepts

Portal of Entry:

Inadvertent or intentional exposures to nanomaterials can be by inhalation, ingestion or via dermal uptake (Fig. 3). In addition, for medical purposes parenteral administration (e.g., intravenous) has to be considered. Examples for unintentional exposures to nano-sized materials include emissions from anthropogenic sources into air (internal combustion engines, power plants, incineration, occupational settings), water and soil (effluents from manufacturing sites, households) or consumer goods (textiles, cosmetics); intentional exposures occur from medications (as aerosols, food additives). Although the development of nanotechnology has increased the potential for exposure of both humans and the environment, nano-sized particles have existed throughout evolutionary stages. While disposition of nanoparticles throughout the body following intake by inhalation and ingestion has been described, although translocated amounts are low, intact skin penetration *in vivo* has not yet been demonstrated. However, miniscule translocation to the dermis in *ex vivo* skin models and in damaged skin (sunburn) has been shown. Methods of exposure to nanomaterials *via* the different routes vary greatly, as does the pre-exposure preparation of NMs. An important question to be addressed, therefore, is the appropriateness of exposure methodology and NM preparation for toxicity testing *in vivo* and *in vitro*.
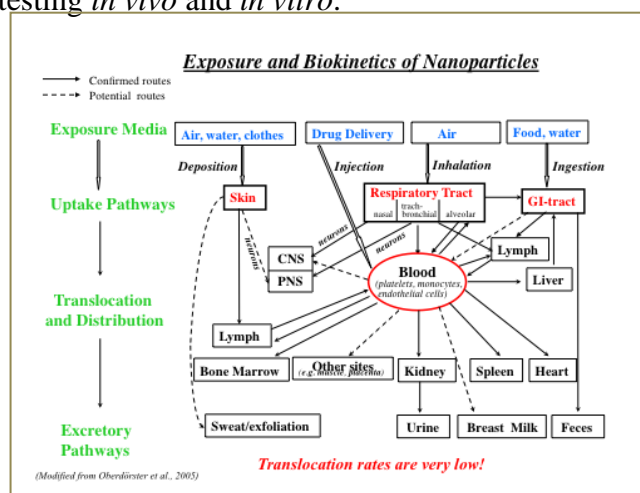

Figure 3

Biokinetics and Dosimetry:

As indicated in Figure 3, the blood compartment is a major compartment of distribution of nanomaterials after their translocation from different portals of entry. Studies with nanoparticles of different physico-chemical properties showed that translocation rates and amounts are very low, such that only between 1-3 percent of nanoparticles depositing in the lower respiratory tract will translocate to the blood circulation, and translocation from the GI-tract seems to be of similar low magnitude. Of importance is also the discovery that nanoparticles do not only cross epithelial and endothelial barriers, but can also be taken up by sensory nerve endings in the upper and lower respiratory tract – and conceivably but yet to be demonstrated in the gastrointestinal tract – and translocate *via* afferent and efferent pathways to central ganglia and the CNS. Studies are underway to assess the implications of such translocation. In general, data that describe the fate of nanomaterials from their absorption at a portal of entry in the body to their excretion (ADME) are of paramount importance for understanding interactions with the organism.

Biokinetics information from appropriately designed studies in laboratory animals is of utmost importance for the planning of *in vivo* and *in vitro* toxicity testing so that the relevance of doses used in toxicity studies can be controlled. For example, the dose of inhaled nanoparticles reaching target cells in secondary organs following translocation from

the lung is 100 or more fold lower than the dose received by lung epithelial cells. However, such differences are neither considered nor discussed when results of toxicity assays are reported that have been performed with doses of many orders of magnitude greater than can realistically be achieved *in vivo*.

As part of biokinetics studies, cellular uptake and intracellular distribution (mitochondria; nucleus) and activation pathways need to be considered (Fig. 4). Again, administered doses are key in terms of cellular effects that are induced by excessive doses due to mechanisms that do not operate at realistic doses *in vivo*.
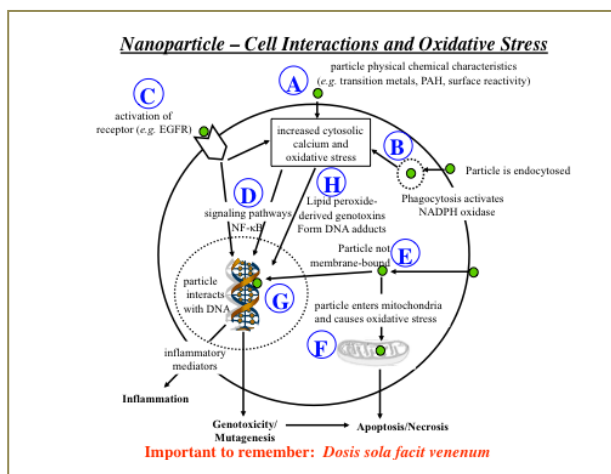

Figure 4

Dose-metrics:

In general, toxicologists express doses by mass. However, given the extremely low mass of nanoparticles and increasing doubts of the usefulness of mass as a metric, other metrics have been proposed, i.e., particle number and particle surface area. For example, the same number of isometric 20 nm gold particles (spec. density ~20 g/cm^3) and isometric 20 nm polystyrene particles (spec. density ~1 g/cm^3) have the same surface area, but 20-fold different masses. Or the greater surface area of the same mass of smaller compared to larger chemically identical nanoparticles makes the smaller particles more reactive, for example as catalyst or also biologically. Indeed, several studies showed that NP surface area appears to be a more useful dosemetric so that normalization to NP surface area, but not to mass or number, resulted in the same dose–response relationship (Fig. 5). However, a more refined version of the surface area concept to be considered as dosemetric is the use of "activity per unit surface area", which will also be useful for establishing a hazard scale and for risk assessment (see below).

It should be noted that biopersistence of a nanomaterial (in the organism, in the environment) plays an important role with regard to dose-metrics. For example, a soluble NP (low biopersistence) will change its physical, and perhaps chemical, properties so that a dosemetric "surface area" or "number" no longer applies. The dissolved mass may then be more appropriate.
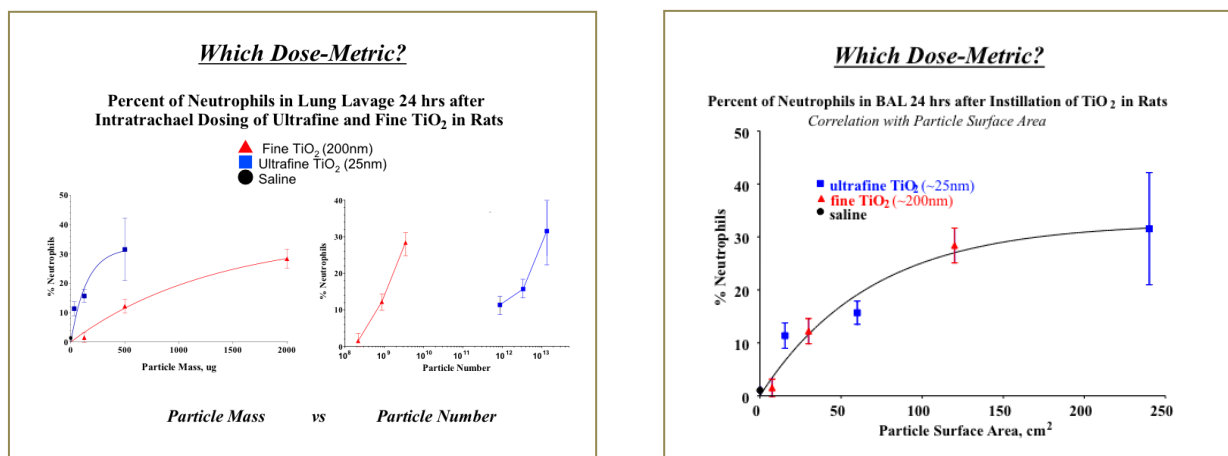
Figure 5

Physico-chemical Properties:

Nanomaterials display a wide variety of physico-chemical properties, all of which can be determinants of biological/toxicological effects. Table 1 lists several of these properties and also indicates that properties change depending on the manufacturing methodology and upon interaction with liquids, as discussed in the following section. Because of the impact of physico-chemical properties on toxicity, it is essential that key properties are determined for any toxicity assessment and be published as a very important part of the test. Obtaining knowledge about changes of these properties when nanomaterials are in contact with biological media or in the organism represents great challenges in terms of improving tools and equipment for detection and measurement of such changes. A high degree of developmental work is required.

Table 1

Protein Adsorption and Impact:

The concept of Differential Adsorption or Protein Corona Formation means that the physico-chemical properties of nanomaterials (Table 1) upon contact with media in specific body compartments (*e.g.,* respiratory tract, GI-tract, blood, extra/intracellular fluid) determine which proteins/lipids adsorb on and desorb from the surface in a dynamic process; this coating then in turn determines the biodistribution of NPs across barriers and in target tissues or cells. Analysis of such formation of a protein corona in plasma showed the existence of an inner "hard corona" with stable and very slowly exchanging proteins, and an outer weakly interacting protein layer rapidly exchanging with free proteins (Fig. 6). Upon

translocation to specific organs the formation of new coronas is to be expected. Research of these phenomena is a high priority, for understanding the fate and effects of nanomaterials. Further research will determine how similar or dissimilar is the formation of the hard corona for different types of NPs, and how different is the corona formation in relevant media other than plasma. The importance of protein corona for purposes of targeted drug delivery across barriers but also for toxicity testing (use of dispersant media, including proteins, prior to testing) need to be evaluated.

Nano – Bio Interactions
Schematic drawing of the structure of NP-protein complexes in plasma:

Two Layers of Proteins of the "Core" Nanoparticle :

An outer "weak" layer of protein corona rapidly exchanging with free proteins *(red arrows)*

And an inner "hard"layer of stable, slowly exchanging corona of proteins
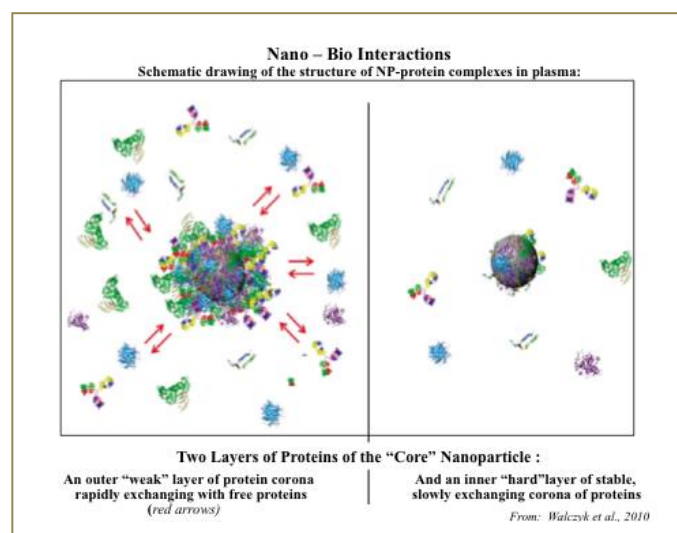
From: Walczyk et al., 2010

Figure 6

Toxicity Testing:

The evaluation of the safety of nanomaterials includes the characterization of their potential hazard that can then be included in the risk assessment process. Tiered testing approaches have been suggested, involving cell-free, cellular and *in vivo* methodologies, perhaps in some distant future to be replaced by *in silico* models. Cell-free assays include the assessment of the inherent capacity of nanomaterials to induce reactive oxygen species (ROS) in a liquid medium; the rationale and hypothesis is that the ROS generating potential correlates with the *in vivo* activity of nanomaterials. There is an urgent need to standardize and validate non-*in vivo* methods for predicting *in vivo* responses, in particular doses/concentrations applied in *in vitro* systems are generally not relevant for realistic *in vivo* exposures.

In vitro studies:
- Cell-free assays:
  – ROS inducing capacity (DCFH assay)
  – ESR
  – Chemical reactivity (Vit C assay)
  – Solubility in simulated body fluids
- Cellular assays:
  – choice of cell types, primary and secondary target organs
  – cell lines; primary cells
  – GI-tract cells
  – lung epithelial cells (tracheal bronchial; type I and 2 alveolar)
  – endothelial cells
  – neuronal cells
  – mesothelial cells

– hepatic cells

– Others …..

Endpoints to be evaluated may be related to induction of oxidative stress, inflammation, genotoxicity and others, depending on study objective. It is essential to design any study by using a wide range of doses that include doses estimated to be relevant and occur *in vivo* (derived from biokinetic studies) so that a careful analysis of the shape of dose-response correlations can be performed (see below). Expressing administered doses as concentration per volume of culture medium or per cultured cell surface area or per number of cells needs to be discussed. Furthermore, the mode of administration as well as the preparation of the nanomaterials to be tested (use of dispersants, sonication) can alter resulting effects and need to be carefully assessed. For example, dosing of respiratory tract epithelial cells either in culture medium or by aerosol via an air-liquid interface model (to simulate in vivo exposure in the lung) can lead to significant differences in response. Table 2 lists justifications and some of the concerns of high dose *in vitro* studies.

Well established *in vitro* methods in toxicology.
But: Concerns about Mega-Doses of NPs without justification

Justification	Concern
reflects dose of repeat exposures and identifies hazard	extremely high dose rate (bolus); not for risk characterization
mimics conditions of susceptibles	dose by orders of magnitude too high
proof of principle study or hypothesis forming study; identifies specific mechanisms	mechanism is dose-dependent; high bolus overwhelms defenses/ adaptive mechanisms
can be developed into high throughput assay	*in vivo* validation required; use of dispersing media is likely to change NP properties
easy to perform with many target organ cells	doses need to consider biokinetics, especially for secondary organs
resembles "hot spots" of deposition in respiratory tract	minor or no "hot spots" for NPs;

Table 2

In vivo studies:

In contrast to *in vitro* assays, studies in laboratory animals will be of a more limited nature given ethical concerns regarding excessive use of animals for toxicity testing as well as associated high costs and the need for specific expertise. However, for validation of specific *in vitro* assays *in vivo* studies are necessary and essential to assure that responses as well as mechanisms observed *in vitro* are also occurring *in vivo*. Depending on the primary portal of entry, methods for dosing vary greatly. For example, if effects of airborne nanomaterials are to be assessed, inhalation exposures are the gold standard as the most physiological exposure method. However, since inhalation exposure requires specific expertise and equipment for aerosol generating, exposing and monitoring, more simple yet unphysiological methods have been designed. Table 3 contrasts the pros and cons of these different dosing methods.

It should be noted that dosing of the respiratory tract also targets the GI-tract *via* efficient clearance of deposited material in the tracheobronchial region *via* the mucociliary escalator to be swallowed. (TO BE ADDED: sentences on oral dosing, gavage ….)

Advantages/Disadvantages of Methods of Dosing Rodent Respiratory Tract with Nanoparticles

Method	Anes-thesia	Deposition throughout Resp.Tract	Evenness of Deposi-tion	Physiol. Mode	Dose Rate	NP Pretreat. to avoid Agglomer.	Stress When Everyday Repeat Exposures	Special Expertise Req'd.
Bolus type Intranasal instillation	Yes	Yes	Uneven	No	High	Yes	High	No
Intratrach. Instillation [a]	Yes	No	Intermed.	No	High	Yes	High	No
Oropharyng. aspiration [b]	Yes	No	Intermed.	No	High	Yes	High	No
Inhalation: [c] whole body	No	Yes	Even	Yes	Low	No [d]	Low	Yes
nose only	No	Yes	Even	Yes	Low	No [d]	High	Yes

a – when synchronized with inspiration; **b** – may cause significant inflammation in rats; **c** – inhalation requires more material; **d** – as dry powder; other aerosolization methods likely to result in significant agglomeration

Table 3

− *In vitro- In vivo* Correlations: Issues that need to be considered are listed in Table 4 below.

In Vitro — In Vivo Correlations

- **Dosimetry issues:**
  - **dose level**
  - **dose rate**
  - **dose-response relationships**
  - **dosing method** (*dispersion; agglomeration*)

- **Endpoints,** *e.g.*:
  - **oxidative stress**
  - **inflammation**
  - **genotoxicity**
  - **cytoxicity**

- **Cell type:**
  - **cell lines**
  - **primary cells**
  - **co-cultures**
  - **organ cultures**

Important: Information on biokinetics, from in vivo studies to assure in vitro–in vivo relevancy

Table 4

Exposure Assessment:
Information about human exposures with regard to dose levels, and nanomaterial physical properties and chemical composition is important for appropriately designing toxicity assays as well as for eventually performing quantitative risk assessment. Measurement of concentrations in air, food and water combined with frequency of exposures *via* different routes will inform toxicologists about relevant and realistic doses to be used for toxicity testing. A major shortcoming is the lack of pertinent information about both acute and chronic exposures. Multiple sources of exposure need to be considered, including potential exposures during different stages of the life-cycle of a nanomaterial. Another difficulty is the lack of knowledge about physico-chemical properties or changes thereof at the time of and during exposure; for example, secondary surface coating/adsorption from air contaminants or from matrix material in food can occur which can be reproduced when toxicity tests are designed and the impact on toxicity outcome can be determined.

Hazard Identification:

One goal of nanotoxicology is to generate data for assessing a potential hazard of nanomaterial using approaches that are outlined in the preceding paragraphs. Although a hazard can readily be identified by cytotoxicity assays, *in vitro* results have to be interpreted with caution with regard to extrapolation to *in vivo* conditions. Whereas studies with irrelevant and unrealistic high doses can be useful as proof-of-principle studies or hypothesis-forming studies, they may not be practical for hazard identification. Questions arise with respect to defining equivalent *in vitro vs. in vivo* doses, or how to interpret and analyze dose–response data when there is a significant response at very high doses but non-significant responses at realistic doses. In addition, the dose-rate *in vitro* is always very high (bolus type delivery), whereas it is generally low *in vivo*.

A careful analysis of dose–response data with consideration of dose- and response-metric needs to be performed with the goal to establish hazard categories. The slope of a dose–response curve is dose dependent (Fig. 7) and so are mechanisms that induce effects. Using the steepest slope as a measure of the maximum response per unit dose seems to be a meaningful approach for comparing *in vitro* and *in vivo* responses. This value can also be used for establishing hazard categories which in turn can be used for classifying new nanomaterials against reference materials of known hazard, low or high. The development of such hazard scale that would allow ranking of tested nanomaterials would be of high value, for example expressing biological activity/toxicity per unit of a nanomaterial surface area. Extrapolation of *in vitro* data involves several steps, from acute *in vitro* to acute *in vivo* to subchronic and chronic *in vivo*, and from animal to human.

Slope (response per unit dose) is dose dependent

$$\text{Steepest slope} = \frac{y_{i+1} - y_i}{x_{i+1} - x_i}$$
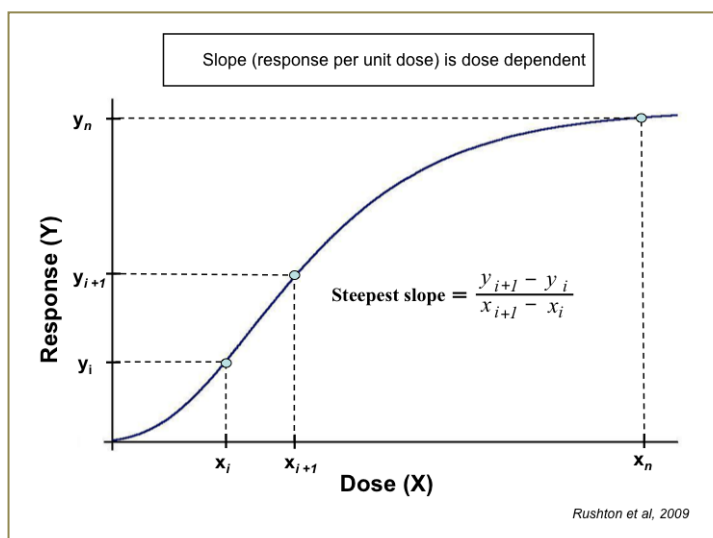
Rushton et al, 2009

Figure 7

Risk Assessment:

The ultimate goal of evaluating the safety of nanomaterials is risk assessment and establishment of safe levels for human exposure or intake. Risk is a function of hazard and exposure, and short-term goals of toxicity testing are directed at defining a hazard (see above) which then together with exposure data can be used for risk assessment purposes. A very long-term goal is to directly use results of *in vitro* assays for predicting safe human exposures. Figure 8 summarizes essential steps and concepts of nanotoxicity testing and its use for hazard identification and risk assessment that were briefly discussed in this paper.
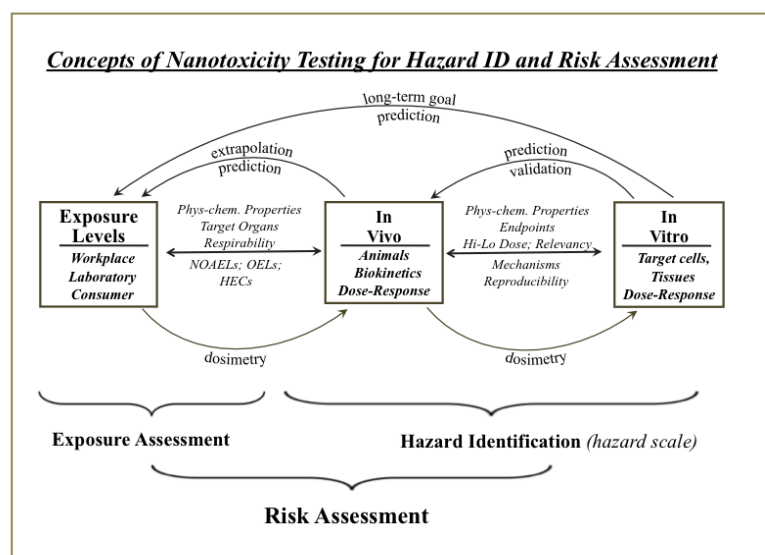
Concepts of Nanotoxicity Testing for Hazard ID and Risk Assessment

Figure 8

<u>Future Goals</u>:

Essential gaps still need to be filled for establishing validated and widely accepted tests for assessing the safety of nanomaterials. These include greater emphasis of dosimetry based on biokinetic data, considering correlations/extrapolations from acute to chronic effects, and developing high throughput assays in order to increase and accelerate performance and efficiency of testing. Key is the validation of predictive testing procedures so that final science-based conclusions regarding human (or environmental) risks from exposure to nanomaterials can be made. An initial assessment of an increased hazard (based on comparison to a known accepted positive or negative reference material) should implement precautionary measures to avoid exposure until a quantitative risk assessment can be performed. Although under expected low exposure conditions most nanomaterials may not pose a significant health risk, more data from chronic exposures are needed to draw final conclusions.

Title: Business perspective on regulatory frameworks and innovation for nanotechnologies

Name: Richard Canady[40]

Introduction

Successfully managed innovation can provide net benefits to the public welfare.[41] Unnecessary inhibition of innovation can therefore have the potential for adverse effects on future public welfare. For this reason, inhibiting effects to innovation should be evaluated for their net benefit. Application of regulatory frameworks to uses of nanotechnology faces at least two challenges that may inhibit innovation. The first challenge is the perception by some, and perhaps many, that regulatory frameworks are not working to manage health and environmental risk for products of nanotechnology. This perception can inhibit innovation because it creates an environment of uncertainty that regulation may be substantially and indiscriminately increased for <u>any</u> material made with the technology. Such an environment of "potential regulatory constriction" can inhibit investment in new product development because there is fear that money will be wasted if products are delayed in authorization or pulled from the market unnecessarily. A second challenge to innovation is the perception that methods for testing and characterizing nanomaterials are lacking. This perception can also unnecessarily inhibit innovation to the degree that it is incorrect for any particular nanoscale material application that provides a net benefit to public welfare. The effects of both challenges can be reduced through specific attention to standardization of methods and evaluation of data that characterize whether exposures occur in real world applications of nanoscale materials.

Challenges to innovation

Perceptions of inadequacy of regulatory frameworks to manage risks. Through the reviews by a number of government regulatory agencies, it appears that there is general agreement that regulators can require the same level of proof of safety for nanomaterials as they can for non-nanomaterials.[42] Therefore, provided that a company does go through the appropriate authorization steps for a food additive made using nanotechnology, then presumably a resulting nanomaterial would be demonstrated to be at least as safe as other materials used in foods that have gone through the same process. Materials that are tested and found to be safe, or that are generally recognized to be safe (by experts who understand effects of the nanoscale properties), should be safe in the meaning of the regulations whether they have nanoscale properties or not. The food additive regulatory change should therefore not differentially provide an uncertain future for nanomaterial development. Once a product made with

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[40] Director, Center for Human Health Risk Assessment. Research Foundation of the International Life Sciences Institute (ILSI)

[41] Considering the impacts of distributed versus individual costs and benefits.

[42] For example, see http://www.wlf.org/upload/07-25-08brown.pdf ; and http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/NanotechnologyTaskForceReport2007/default.htm and a US government-wide evaluation in 2007 titled "Principles for Nanotechnology Environmental, Health, and Safety Oversight." which concluded that "The Federal government's current understanding is that existing statutory authorities are adequate to address oversight of nanotechnology and its applications. As with any developing area, as new information becomes available the Federal government will adapt or develop additional oversight approaches, as necessary, to address the area of nanotechnology." However, also note that the Food Safety Authority of Ireland concluded that regulatory mechanisms are insufficient. http://www.fsai.ie/WorkArea/DownloadAsset.aspx?id=7858

nanotechnology goes through the data review and authorization processes, it should be as safe as any other product.

So why is there uncertainty about whether regulation is adequate to address products of nanotechnology? Press accounts refer to nanomaterials in products as though there are unevaluated materials in the foods that are likely to be a risk to health.[43] The press accounts do not refer to regulatory agency evaluations of their own regulations, or of the authorization history itself for particular materials. Where is the disconnect happening? What data or evaluations could bridge the gap in understanding?

Similarly, reports in policy review and opinion literature state that "oversight implementation" is challenged by nanotechnology, and further say that entirely new legislation is needed to address nanotechnology.

> *Oversight of new technologies in this century will occur in a context characterized by rapid scientific advancement, accelerated application of science and frequent product changes. The products will be technically complex, pose potential health and environmental problems and have an impact on many sectors of society simultaneously. They may also raise challenges to moral and ethical beliefs. Nanotechnology embodies all of these characteristics as well as particular ones that challenge conventional methods of risk assessment, standard setting and oversight implementation.[44]*

Therefore despite evaluations by those on the front-lines at the regulatory agencies that the regulatory frameworks are as adequate for the products of nanotechnology as they are for any other materials, it is apparent that uncertainty remains in the minds of some, and perhaps many, as to whether regulation is effectively applied to the uses of nanotechnology in foods.

The perception that there is harm due to inadequate regulatory oversight is difficult to address in the face of a lack of information that exposures to nanoscale materials have or have not occurred, or furthermore that harm has or has not occurred because of materials made with nanotechnology in foods. The concern about potential adverse effects is based entirely on what could hypothetically happen in products rather than a demonstration of harm for any particular product. The concern furthermore is based on speculation that the harm shown under specific controlled laboratory conditions for some nanoscale materials applies to entirely different conditions for other materials in food or food contact material matrices. Therefore, those wishing to innovate using nanotechnology are effectively faced with proving a negative (to investors) that risk does not exist in the abstract and general case of all nanomaterials, before they can develop a product to test for toxicity or risk.

Obviously it is impossible to develop information regarding risk of all nanomaterials because the set of all nanomaterials is an infinite set, and therefore the product developer's task of countering the claims of inadequate regulation is an impossible one. However, there are likely to be general characteristics of some material types or some material uses that may provide indications of greater or lower risk that can begin to change the generalized perception of harm and lack of regulation into a body of knowledge about specific areas of application.

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[43] http://www.aolnews.com/category/nanotech/
[44] http://207.58.186.238/process/assets/files/7316/pen-18.pdf

Lack of clarity regarding what methods can be used to support risk management decisions.
Some part of the perception of regulatory framework inadequacy can be attributed to perceptions that there is a lack of methods to characterize nanoscale materials in products, the environment, or our bodies.[45] The general case has been made in review documents by government agencies, advisory bodies, and others that methods do not exist, that methods are needed before testing can be done properly, and that because of a lack of such methods we do not know true exposures or risk. The challenge to innovators in this case is either to demonstrate to investors that existing methods are adequate to support the risk management decisions for a specific product, or to develop new methods as they also develop the product.

However, it is possible that in many cases where nanotechnology has been used that existing methods will provide most if not all of the needed data to make risk management decisions. For example, existing methods may be sufficient in categories of nanomaterial use where the material enters into a matrix and can be demonstrated to not exit as a nanomaterial (although the initial demonstration of the lack of release as nanomaterials could require nanomaterial-specific methods). For example, structural components of containers added during fabrication that become bonded to a matrix could be demonstrated to not leave the matrix as nanomaterials.[46] Standard chemical analytical methods should suffice once the material has been added to the matrix in these cases where there is no subsequent exposure to a nanomaterial. Therefore, it seems possible that a substantial amount of the evaluation of nanomaterial use in foods could be addressed using existing methodologies, and if that were the case then the perception that new methods are needed would be an unnecessary inhibition to the development of products using nanotechnology. Guidance to determine when such conditions exist could therefore substantially improve the likelihood that a product is worth investing in.

Lack of guidance or standards regarding what nanoscale data and reporting will be accepted by regulators to support risk management decisions. On the other hand, new methods will be needed to characterize particles with nanoscale characteristics in those cases where exposures to the nanomaterials are expected. A factor complicating the development of products is that there is a range of possible new methods for measuring specific nanoscale characteristics. Because it is not clear what methods will be preferred or required by regulatory agencies, there is a risk that any data developed now during product development may prove to be irrelevant. This risk again provides an inhibitory influence on investment.
For example, the Nanotechnology Characterization Laboratory of the US National Cancer Institute has found that size reported for particles can vary depending on the instrumentation and preparation methods used.[47] Therefore the choice of which method to use may play a critical role in the evaluation of data. Furthermore, there is also a range of possible characteristics and their "measurands"[48] to report about a particular nanoscale material. The

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[45] See for example, http://www.fsai.ie/WorkArea/DownloadAsset.aspx?id=7858 ; http://www.fda.gov/ScienceResearch/SpecialTopics/Nanotechnology/NanotechnologyTaskForceReport2007/default.htm ; http://www.nano.gov/NNI_EHS_Research_Strategy.pdf

[46] US EPA has indicated in responses to some pre-manufacturing notifications that polymer matrix bound carbon nanotubes are an acceptable form for commercial distribution but free carbon nanotubes may not be, indicating that a lower risk is expected from the polymer bound forms.

[47] For example, see reports on solvent and temperature effects on size for dendrimers and ceramide liposomes
http://ncl.cancer.gov/working_technical_reports.asp

[48] Definitions of measurand on the Web:

Organisation of Economic Cooperation and Development's Working Party on Manufactured Nanomaterials (OECD WPMN) and the International Organization for Standardization (ISO TC 229) have been working on a list of about 16 characteristics that should be reported in studies; however, there is no general acceptance or guidance specifying that any particular characteristic or measurand should be used. Because of this variability, the reported data for a study (for example a toxicity study) can vary substantially for nanomaterials, so that the ability to compare results between studies can be substantially limited.

Strategies to overcome the challenges

Developing a body of knowledge showing product categories where there is little likelihood of harm (proving a negative). Data showing whether and how exposures occur for specific product types that are likely to be developed would have a stimulating effect on product development. For example, if nanoclays are being proposed for use in packaging then generalized information about the release of nanoclays as nanomaterials could be developed for various polymers. Some information like this has already been generated, and perhaps the best approach would be to simply collect it with respect to particular hypotheses (for example, do nanoclays migrate to food from polymer matrices) determine the gaps in understanding relevant to anticipated product uses of the material, and propose research to fill the gaps. Generalized principles of aggregation and of factors that increase or decrease release from matrices could also be developed around specific kinds of applications. As data are generated about types of specific applications, the perception of "all nanomaterials are un-regulated" may change to a discussion of particular applications and how to manage the risks for them.

Development of generally accepted and widely-used standards of measurement and reporting for "nanoscale elements" of materials. Stakeholders should develop standard methods of data development and reporting so that data can be compared and so that data developed now will be less likely to be obsolete. This is an area of active development by OECD WPMN and ISO TC 229 and should be further addressed through development of international guidance for specific application to assessment of nanomaterials in foods. To encourage utility of academic research in regulatory decision-making, mechanisms such as grants approvals, journal submission rules, and regulatory guidance should be coordinated so that all are requiring the same sets of information in studies. Stakeholder involvement should be encouraged so that the specific products being developed for food applications can be considered in the development of such guidance and practices.

Conclusion

Through the development of such standards of measurement and reporting and development of knowledge of release and exposure it will possible to reduce barriers to innovation while providing for safe use of nanotechnology.

"A quantity that is being determined by measurement."
http://en.wiktionary.org/wiki/measurand
"The physical quantity, property, or condition which is measured. (eg: pressure, load, weight, acceleration)." www.endevco.com/resources/Glossary.aspx
"The particular quantity or subject to be measured under specified conditions; a defined set of specifications for a measurement application." www.measurementdevices.com/index.php

Title: A consumer group's point of view on the regulatory framework and nanotechnologies
Name: Sue Davies[49]

Introduction

The use of nanotechnologies in food and agriculture has the potential to offer consumers a range of benefits, but could also present new risk unless developed responsibly and effectively regulated. At the moment it is difficult to assess the full implications of the technology. Fundamental knowledge gaps exist around what is already on the market and under development. There are also gaps in basic research which make it difficult to ensure robust risk assessment and the adequacy of regulatory oversight. These issues need to be urgently addressed and a more strategic approach adopted in order to ensure that nanotechnologies are developed safely and responsibly so that consumers can take advantage of the benefits without being put at unnecessary risk.

Key issues

Transparency

Many potential benefits from the use of nanotechnologies in food and agriculture are claimed, from improving quality and shelf life to nutritional benefits. But there is very little information about what is happening in reality, including what is already or close to coming on to the market and what could be seen in the future. The mainstream European food industry has stated that it is not currently using nanotechnology (UK House of Lords 2010), but a quick trawl of the internet reveals several products such as food supplements claiming to be using nanotechnology and available for consumers to buy.

The issue is compounded by a lack of clarity over what is classed as nanotechnology. International consensus is needed around working definitions, but this must not delay action to understand the status of developments and ensure that any risks are dealt with effectively. There now appears to be general acceptance that both size and functionality need to be taken into account.

This lack of transparency is problematic not only from a regulatory point of view, in that it means that it is difficult to ensure the adequacy of risk assessment and management measures, but also because it prevents meaningful, two-way risk communication.

Engagement

Public engagement in this area is essential on a number of levels. Consumers have a very personal relationship with what they eat and therefore have a right to know about key developments in the food chain and make informed choices about them. Effective engagement is also essential in order to ensure that the development of the technology and how it is regulated is in line with society's expectations and any concerns are addressed. There may be applications that consumers are particularly enthusiastic about, but it is also important to understand the limits of acceptability. Public acceptance is key to the successful development of a technology, as seen with the introduction of other novel technologies, most notably genetically modified (GM) foods. Failure to address consumer concerns can lead to a breakdown in confidence and trust in both the industry and regulators. As highlighted in the recent UK House of Lords' report into nanotechnologies and food (UK House of Lords 2010), an appearance of secrecy by the food industry is "*exactly the type of behaviour which may bring about the public reaction it is trying to avert*".

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[49] Which?, UK

Research conducted by Which? in the UK has found that there is generally a low level of awareness of nanotechnology by consumers. A survey in 2007 (Which? 2007) found that 37 per cent had heard of nanotechnology. This had only increased slightly to 45 per cent in October 2008 (Which? 2008). Engaging the public can therefore be difficult. In November 2007, Which? organized a citizens' panel in order to try and gain a greater insight into people's reactions to the use of the technology, focusing on four main areas of development: food, medicines, cosmetics and general consumer products (Which? 2008a). The panel met over three days and heard evidence from a range of experts. This process indicated that despite coming from a range of backgrounds, people did become very engaged with the issues. They were open to developments, including in the food area although this is most sensitive, provided they are assured that there is an adequate regulatory framework in place to ensure the safety of products and enable informed choices.

The Which? research found that trying to ground public dialogue in specific examples as well as providing clear information about the different regulatory regimes enabled a fuller and more meaningful dialogue. The main recommendations from the panel are set out in Figure 1. In general the people involved were surprised that the technology was so advanced, although they had not heard of it, and they wanted the government to take a more comprehensive and strategic approach to its oversight, as summed up by the following comment from one of the respondents: "*It's like going out blindly into a blizzard – or actually sitting down with a map and thinking about where you are going to go*".

Main conclusions from the Which? Citizens' Panel on Nanotechnologies (2008)

Safety: Panellists were concerned that products are on the market when scientists are uncertain of their safety.

Lack of regulation: Participants wanted regulation to deal with the risks nanotechnology raises and stressed the need for international action.

Information: There was concerned that there is no requirement to inform consumers about products using nanotechnologies.

Accessibility: It was questioned whether beneficial uses of nanotechnology would be accessible to all.

Environment: There was concern and interest in possible environmental impacts.

Ensuring safety

Unsurprisingly, safety was a major concern for the people involved in our research. Numerous reports from leading expert bodies since the UK's Royal Society and Royal Academy of Engineering reported in 2004 (Royal Society/Royal Academy of Engineering 2004) have stressed that the novel properties of nano materials could present new risks as well as benefits and highlighted the need to address fundamental research gaps in order to enable effective risk assessment. While generally it is recognized that the current approach to risk assessment can be applied to nanotechnologies, key uncertainties in areas such as hazard characterization and exposure assessment (EFSA 2009) make it difficult to be clear about the potential risks. These gaps are still not being addressed with sufficient urgency.

This raises fundamental challenges for the regulatory framework: it is essential that given their novel properties nano materials are subject to a pre-market safety assessment, but there are still outstanding questions about how that assessment should be conducted and how any requirement can be effectively enforced given the lack of clarity about market developments. As recognized within the Codex Working Principles for Risk Analysis (Codex 2007), it is also important that approval processes also take into account 'other legitimate

factors', which include broader social and ethical considerations, when determining whether a product should be placed on the market. Effective risk communication is essential in order to understand what these factors may be.

While debates around definitions, risk assessment and regulatory frameworks continue, consumers ultimately rely on enforcement officers at the local level to ensure that legislation is effectively enforced and that they are adequately protected. It is therefore important that legislative requirements are translated into clear guidance for enforcement bodies, as well as the food industry, so that once adopted, legislation is also complied with. Which? has for example found problems in the cosmetics area, where the safety of nano materials used in certain cosmetic products has been questioned by the EU's Scientific Committee on Consumer Safety, but there is a lack of awareness at a local authority level, making it difficult to ensure that potentially unsafe products are removed from sale.

Information, labelling and claims
Regulators also have a responsibility to ensure that the public is adequately informed about the use of nano materials in products. This is a difficult area as the usefulness of product labelling is often questioned in light of limited public awareness, leading to a circular discussion. However, consumers generally wish to know about the use of new technologies in food production and therefore it is important that they have clear information, supported by broader awareness raising of nanotechnology. Transparency across the supply chain is also essential in order to ensure that all actors are aware of the use of nano materials.

It is also important that products that claim to be produced using nanotechnology, actually are. While some manufacturers currently appear to be trying to avoid any association with nanotechnology; other products are actively promoted on this basis. It is therefore essential that consumers can trust any claims made about potential benefits on products and in associated advertising material. Where products do offer genuine benefits, accessability is also an issue. As highlighted by the people in the Which? citizens' panel: "*Inclusiveness is important – that these changes and applications make everyone's lives better*".

Challenges identified
They key consumer questions that arise in relation to the use of nanotechnologies can, therefore be summarized simply as follows:
- where are nano materials being used?
- how can consumers find out?
- how can we ensure or assess their safety given key knowledge gaps?
- how can consumers have a say in the development of the technology?
- which applications will bring genuine benefits?
- can consumers trust the claims some products are making?

Addressing these issues is compounded by the global nature of food production and supply and the increasing availability and purchase of products over the internet. International collaboration is essential in order to ensure that there is consistent and effective consumer protection around the world. It is also essential in order to fully understand what types of developments are taking place, those of most and least concern, to take advantage of genuine opportunities to help tackle the major challenges facing the food chain including food sustainability, non-communicable diseases, food safety and food security.

However, the benefits of international co-operation and co-ordination should not delay the important actions that need to be taken by national and regional governments in order to ensure that nanotechnologies are developed and used responsibly in food and agriculture. While there may be benefits in taking work forward through Codex, for example, to provide guidance on risk analysis for member governments, Codex's decision-making processes are slow and can all too often be weakened by too much focus on trade interests at the expense of consumer protection.

Strategies to overcome the challenges

Transparency

Poor experience of the introduction of other food technologies has meant that the food industry appears wary of speaking openly about its use of nanotechnology. This can only be counter-productive. If nanotechnology does have the potential in many areas as predicted, consumers should be made aware of this. Failure to be open about developments will arouse suspicion rather than prevent it.

It is therefore essential that the food industry is more open about its developments and that there is clear communication about the use of nano materials across the supply chain. Attempts at encouraging voluntary reporting of the use of nano materials, for example the UK's voluntary reporting scheme, have not been effective with very limited disclosure of information. It is therefore essential that governments introduce mandatory reporting schemes in order to enable them to assess the implications from a regulatory and risk perspective. This information also needs to be communicated in a more general form to consumers.

Policy makers also need to work with industry to determine the likely course of developments over the next 5, 10, 20 years and beyond, including possible applications of most and least risk and determine how the technology can be aligned with the main public policy challenges from obesity to climate change.

Engagement

The FAO/WHO expert consultation on nanotechnologies (FAO/WHO 2009) recognized the value and importance of effective stakeholder dialogue including that with the general public. There have been various initiatives, using different deliberative techniques from the type of Panel organized by Which? to larger, national debates which have met with varying degrees of success.

There needs to be an effective high-level dialogue between key stakeholders in order to assess the status of developments. But a wide range of techniques also need to be used to more effectively listen to, understand and respond to consumer reactions to developments at all stages of decision-making. This requires greater sharing of information and exchange at all stages of risk analysis. It also needs to focus on specific applications in order to better understand public priorities.

Ensuring Safety

Research needs to be further co-ordinated so that gaps can be addressed as a priority and a harmonized approach to risk analysis agreed, including agreement on working definitions while allowing some flexibility for them to be revised as understanding improves.

Gaps in regulations need to be urgently addressed so that nano materials have to be independently assessed and approved before marketing. Existing Codex guidance on risk analysis is important in this respect, but should be supplemented with more specific standards. Clear guidance also needs to be provided for industry and enforcement officers so that legal obligations are clear. Where there is uncertainty about safety, products should not be allowed on the market.

Many food applications that are relevant to the use of nanotechnology are, for example, subject to specific legislation in the European Union that requires a pre-market authorization, including a risk assessment by the European Food Safety Authority (EFSA). Much of this has been, or is in the process of being updated to take account of the specific properties of nano materials and to clarify that materials in nano form require separate approval to their conventional form. The novel foods regulation is currently under review and there is support from both the European Parliament and Council to explicitly address the use of nanotechnologies. It is essential that there is clarity across all legislation relating to potential areas of application and that legal requirements are also translated into clear, unambiguous guidance for industry and enforcement officers.

Information, labelling and claims

Labelling of nano ingredients in the ingredients list should be a legal requirement, backed up by broader consumer information. This is now a requirement for cosmetic products in the European Union so it would be difficult to argue that consumers should not have the same information about ingredients used in food.

It is essential that genuine benefits are realized and offered to consumers. Involving consumers at an early stage when determining research priorities should help to ensure this. Broader social and ethical issues also need to be taken into account as part of the risk analysis process, in line with Codex guidance on the role of other legitimate factors. Claims about potential benefits also need to be substantiated and effectively policed by national authorities to ensure that consumers are not misled.

Conclusion

Nanotechnologies have the potential to offer consumers many benefits, but this will not be realised unless key research, risk assessment and regulatory gaps are addressed with greater urgency. Much greater transparency is needed around the status of developments in order to ensure effective regulatory oversight and meaningful public engagement.

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8. Which? (2008) Face to face survey of 977 adults aged 16+ representative of adults in the UK in October 2008.
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Annex IV
Technical Round Table Sessions Agenda

Tuesday 22 June 2010

Time	Plenary			
14:00-14:10	Plenary Opening			
14:10-14:20	Brief introduction of 3 round tables, structures, objectives and expected outcomes			
14:20-14:30	*Break*			

Time	Round Table 1 (FAO/EFSA)		Round Table 2 (FAO/IUFoST)	
14:30-15:15	Identifying the key issues	RT experts (each to make 5-min presentation)	Identifying the key issues	RT experts (each to make 5-min presentation)
15:15-16.00	Open discussion	All	Open discussion	All
16.00-16:15	*Break*			
16.15-16:45	RT discussions identifying the strategies and follow-up actions	RT speakers	RT discussions identifying the strategies and follow-up actions	RT speakers
16:45-17.30	Open discussion	All	Open discussion	All
17.30-18.00	Wrap up and conclusions	RT speakers	Wrap up and conclusions	RT speakers
18:00-18:10	Final remarks	RT 1 Chair	Final remarks	RT 2 Chair

Wednesday 23 June 2010

Time	Plenary	
14.00-14.20	Brief presentation of RT1+2 outcomes	RT 1 and RT 2 Chairpersons
14.20-14.30	*Break*	

	Round Table 3 (FAO/OECD)	
14.30-15:15	Identifying the key issues	RT experts
15:15-16:00	Open discussion	All
16:00-16:15	*Break*	RT speakers

16:15-16:45	RT discussions identifying the strategies and follow-up actions	All
16:45-17.30	Open discussion	All
17.30-18.00	Wrap up and conclusions	RT speakers
18:00-18:10	Final remarks	RT 3 Chair

Thursday 24 June 2010

Time	**Plenary**	
14.00-14.20	Round Table 1 Presentation	RT 1 Chairperson
14.20-14.30	Q and A	All
14.30-14.50	Round Table 2 Presentation	RT 2 Chairperson
14.50-15.00	Q and A	All
15.00-15.20	Round Table 3 Presentation	RT 3 Chairperson
15.20-15.30	Q and A	All
15.30-16.30	*Break for audience, RT members to work on the overall document*	
16.30-17.00	Conclusions and way forward	All RT Chairpersons

Annex V
List of Round Table Sessions Participants

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