Organisation de Coopération et de Développement Économiques
Organisation for Economic Co-operation and Development

25-Sep-2014

English - Or. English

Directorate for Science, Technology and INNOVATION
Committee for Scientific and Technological Policy

DSTI/STP/NANO(2013)10/FINAL
Unclassified

Working Party on Nanotechnology

NANOTECHNOLOGY IN THE CONTEXT OF TECHNOLOGY CONVERGENCE

JT03362474

Complete document available on OLIS in its original format

English - Or. English

FOREWORD

Converging technologies are surrounded by big promises concerning, for example, a third industrial revolution, a sustainable world, and human enhancement. However, while the rhetoric surrounding converging technologies is attractive, it can at the same time be an obstacle to the realisation of envisaged benefits because its rather diffuse and open-ended nature makes it difficult to decide in which direction to go and which initiatives, products and processes to invest in or adopt.

Nanotechnology (here encompassing both nano-sciences and nano-technologies) has been identified by some as a cornerstone of various visions of converging technologies. It has evolved from a promising area in the early 2000s, to a thriving multi-disciplinary field of research and development (R&D). There are dedicated research centres, emerging supply chains (resulting from a scaling up of nanomaterial production) and multiple applications, in areas ranging from medical applications to food packaging.

This report explores the characteristics of nanotechnology as it relates to technology convergence i.e. actual instances of the convergence of different technology streams in the research and innovation environments within laboratories and companies. It examines four application areas in which nanotechnology plays a strong role (green packaging, food safety and security, pharmaceuticals and medical devices). It has been developed by the Secretariat of the Working Party on Nanotechnology (WPN) with inputs from Christien Enzing (Technopolis B.V.) and Douglas K. R. Robinson (Teqnode B.V.).

This report is the final output of work conducted on nanotechnology in the context of technology convergence within the 2011-2012 Programme of Work and Budget (PWB) of the Committee on Scientific and Technological Policy (CSTP). The Committee approved this report on 9 December 2013.

TABLE OF CONTENTS

Figures

Tables

EXECUTIVE SUMMARY

Converging technologies and **NBIC** (nano, bio, ICT and cognitive sciences) are umbrella-terms commonly used when considering the integration of different scientific disciplines and their technological applications, generally with the aim of adding value. The terms are used routinely in policy circles when discussing future options and priorities, formulating policies and implementing new support programmes. The potential of converging technologies to transform industry and society has been much discussed since the early 2000s, firstly in the context of human enhancement[1] and secondly where they may offer potential solutions to societal grand challenges.

Technology convergence, on the other hand, refers here to specific examples of actual convergence between particular technologies and the way this convergence manifests itself in terms of the impacts on research activities in laboratories and companies and the development of scientific and technological communities.

Converging technologies are surrounded by big promises concerning, for example, a third industrial revolution, a sustainable world, and human enhancement. However, while these promises are attractive, they can at the same time be an obstacle to the realisation of envisaged benefits because their rather diffuse and open-ended nature can make it difficult to decide in which direction to go and which initiatives, products and processes to invest in or adopt. This leads to a gap between the generic, high-level promise of converging technologies, which is often couched in terms of the resolution of global challenges, and the specific promise of individual examples of technology convergence in the laboratory. The promises and projections of **converging technologies** often do not take into account the realities of designing and manufacturing marketable products from instances of **technology convergence**.

This report explores the characteristics of nanotechnology as it relates to technology convergence, examining four application areas in which nanotechnology plays a strong role (green packaging, food safety and security, pharmaceuticals and medical devices).

By focusing on these instances of technology convergence, the report highlights that:

- There are multiple ways in which nanotechnology may be involved in technology convergence e.g. as an enabler for developments in other areas of science and technology (e.g. pharmaceuticals) or as a final product with enhanced properties through nanotechnology (e.g. in food packaging or drug delivery).

- A number of impact pathways are presented in the main body of the report. These vary in terms of how and where the nanotechnology is used. They span different industrial domains (e.g. energy applications, medical and sensing technologies, food processing, and packaging) and different positions in the value chain from the research stage to final use of a product.

- A key challenge is to characterise these impact pathways and develop appropriate impact indicators (e.g. to assess where the main impacts occur and to measure these impacts in terms of technical improvements, reduced costs, improved use of resources and/or environmental health and safety effects, amongst others).

- Based on such assessments, policy interventions concerning nanotechnology-related technology convergence might best be focused:

1. - On specific instances of convergence (e.g. on specific research fields like nanobiotechnology or synthetic biology);

2. - Along particular value chains (e.g. neurotechnology and targeted drug delivery); or

3. - On attempts to embed technologies into particular application areas corresponding to societal needs (e.g. green packaging).

However, policy makers should apply caution when interpreting and using the findings of this report. The design of policies catering for emerging and converging technologies is complicated by the rapid pace of innovation and change. Country and regional variations are also likely to be considerable.

If the generic promises of converging technologies are to be realised, successful policy measures will also need to take societal concerns about particular instance of technology convergence into account.

I. CONVERGING TECHNOLOGIES AND TECHNOLOGY CONVERGENCE – THE EXAMPLE OF NANOTECHNOLOGY

Introduction

Converging technologies offer possibilities to add value through the integration of different scientific disciplines and their technological applications. Convergence in areas of technological development has promised potentially transformative changes to industry and society since the early 2000s. This was initially with projections of significant contributions to human enhancement and more recently, by promising potential solutions to societal grand challenges (Milleson, 2013).

Nanotechnology (here encompassing both nano-sciences and nano-technologies) has been identified by some as a cornerstone in various visions of converging technology. It has evolved from a promising area in the early 2000s, to a thriving multi-disciplinary field of research and development (R&D). There are dedicated research centres, emerging supply chains (resulting from a scaling up of nanomaterial production) and multiple applications, in areas ranging from medical applications to food packaging.

As a wider enabling technology, nanotechnology adds value through its combination with other technologies in a variety of ways. However, this wealth of possible combinations and potential application domains creates challenges as well as opportunities. This report will explore these via the use of Case Studies and, based on these practical examples, highlight common issues where further policy consideration may prove useful.

Converging technologies and NBIC as visions

The umbrella terms "Converging Technologies" and "NBIC" – combinations of nanotechnology (N), biotechnology (B), information and communication technologies (I) and cognitive technologies (C) - have been commonly referenced over the past decade or so. In the early 2000s, the NBIC initiative of the United States triggered much debate and was closely tied to forward-looking activities related to nanotechnology, particularly around the vision of human enhancement applications.

The research arm of the European Commission (then DG Research) noted the interest generated in the US and developed more specific descriptions in the area. It initiated an activity that led to the 2004 CTEKS report (Nordmann 2004) which extended "converging" to all sciences and technologies, and developed the concept of a governance approach[2] for this field of work.

A similar approach to convergence was taken in a report commissioned by the European Parliament and undertaken by the European Technology Assessment Group (ETAG, 2006) and other actors also began to discuss topics related to converging technologies. For example, the International Risk Governance Council (IRGC)[3] and the European Group on Ethics.[4]

Now the term NBIC itself has evolved in the form of NBIC2,[5] which has broadened the original term to include more disciplines and to consider the issues of convergence on much greater scales than research or technological development alone.

Technology convergence as a process

Entangled with the notion of **converging technologies** is the notion of **technology convergence**, where scientific disciplines or key enabling technologies combine with other disciplines or enabling technologies to promise new or added-value beyond synergies. Technology convergence has been visible in nanotechnology itself, for example in the convergence of disciplines (e.g. physics, chemistry, engineering) at the nanoscale (Robinson et al., 2007).

Technology convergence is distinct from the notion of converging technologies in that it refers to specific instances of convergence at the level of research and innovation activities, whereas the term converging technologies is most often used in policy circles when formulating and implementing policies aimed at realising high-level societal objectives via the integration of technologies. Technology convergence is more than just a combination of different disciplines or technologies. Value is added through convergence, resulting in completely new ideas, methods and outputs.

Technology convergence is frequently used to describe the process of actual research and innovation activities in laboratories and in firms. It incorporates the general idea that technology convergence is the transformation of multi-disciplinary activities into inter-disciplinary activities.[6] In inter-disciplinary activities, previously separate disciplines come together synergistically to form a new type of activity. While multidisciplinary activities with experimental synergies can result in enhancements in research and development, they do not possess the originality and depth of potential of inter-disciplinary activities.

True inter-disciplinarity within technology convergence can result in previously unexplored areas of experimentation and new ways of working. Taking the results of technology convergence from the laboratory into development, demonstration and deployment can bring industry into new realms of manufacturing and offer new products. These in turn can have new and unforeseen benefits for society if developed in a responsible manner.

Issues for consideration (in this report)

While it is unclear how much knowledge creation and product development is actually linked to policy efforts aimed at realising high-level societal goals via **converging technologies** and NBIC, there is some evidence that actual instances of **technology convergence** and inter-disciplinarity in some areas of research and innovation are leading to value creation in laboratories and in firms.

Within the context of technology convergence, Section II looks at application domains in which nano-involved convergence is taking place or is promising to create an impact. It examines four examples of application domains in which nano-related convergence is occurring. These are: green packaging; pharmaceuticals; medical devices; and food safety and security.

Section III then draws on the evidence and analysis presented to identify key issues and policy implications for nano-related technology convergence and, where possible, considers how they might be addressed.

II. EXAMPLES OF NANOTECHNOLOGY-RELATED TECHNOLOGY CONVERGENCE

The four nanotechnology application/domain areas examined in this section, as particular instances of convergence, are:

- Sustainable and green packaging (using nanobiomaterials).
- Targeted drug delivery and controlled drug release (using nanoparticles).
- Neurotechnologies for health and well-being (using nanomaterials and sensors).
- Food safety and security (through advanced sensors).

To allow for a systematic approach in exploring these diverse domains, each example is structured as follows:

- Overall policy driver – the promise (why people are interested).
- Scientific research.
- Product development and manufacturing.
- Impacts on society, public debate and governance.

Sustainable and green packaging

In this example of green packaging materials, technology convergence is visible in the form of nanobiomaterials and their applications. There is a large and varied research landscape in this area with product development underway, though challenges remain in commercialisation and wider embedding of the technology. The example was chosen to illustrate the dynamics in an active field of technology convergence involving nanotechnology

Overall policy driver: The promise (why people are interested)

The volume of waste generated by the global agri-food sector is of increasing concern. In Europe alone, the fruit and vegetable industries generate around 30 million tonnes of waste per annum. Food packaging waste is predicted to increase as a result of the increasing demand for convenience food and for individual wrapping of fresh produce (such as fruit). One recent example of a pledge to address this issue is in the United Kingdom where the Government stated that, in 10 years' time, 75% of all household waste should be recycled and that *"Early next year we will consult on what recyclable and compostable items should be banned from landfill and how a ban will work,"* (DEFRA, 2011).

Also in the United Kingdom, approximately 10.5 million tonnes of packaging enters the waste system every year (DEFRA, 2011) with more than half of this related to food and drink. The cost of related raw materials is around EUR 4.5 billion per annum. Furthermore, this figure does not include disposal and recovery costs, or wider social and environmental costs such as the accumulation of plasticisers in underground water and the production of dioxins by, for example, the incineration of PVC and paper-based packaging materials. This not only means that there is a real incentive to address the challenge of packaging waste management, but also illustrates the size and range of the problem. The waste

management solution (or portfolio of solutions) should be aligned with food packaging material options (and vice versa).

Bio-sourced and biodegradable packaging materials have been identified as having the potential to address this challenge. Sustainable sourcing of packaging material could be used in conjunction with packaging that decomposes into nutrients to replenish further crops of bio-sourced materials. However, standard bioplastics[7] (another term is biopolymer) have not as yet been able to compete with fossil-fuel based plastics in terms of functional properties. They lack the necessary strength and impermeability to water and/or gas (important not only for drinks but also for food preservation).

Nano-biomaterials have been shown to provide the packaging material functionalities needed to compete and potentially replace fossil-fuel based packaging materials. Since this area of material innovation is the coming together of nanoscience and biomaterials, the consequences of this relatively clear instance of nano-involved convergence are explored below. This section presents three areas in which nanobiomaterials offer useful options for food packaging: 1) bionanocomposites; 2) bio-based nanofibres; and 3) edible films and coatings. There is also a sub-section on product development, where activities to create mass production capacity for some of these materials and compete with more traditional fossil-fuel based materials are in evidence.

Scientific research

Bionanocomposites

For many plastics, recycling is difficult as a result of the mix of materials involved. This often means the item cannot be processed in a single step, instead needing to be separated into component plastics. A better alternative may be to biodegrade the plastic rather than recycle (though recognising this may require new infrastructure). Such biodegradable plastics would be based on proteins or sugars derived from animal or plant sources (Robinson and Salejova, 2010).

When biopolymers (such as cellulose) are mixed with nanoclay particles, the resultant nanocomposites can exhibit better water and gas permeability properties than the pure polymer, and, after their useful life, can be composted and returned to the soil (Zhao et al., 2008). Polylactic acid (PLA) is a bioplastic with significant anticipated potential for commercialisation, mainly due to its ease of production from carbohydrate feedstock such as maize, whey, wheat or molasses (Zhao et al., 2008). Combining bio-based materials with nanomaterials or manufacturing them using nanoprocessing opens up many potential applications, possibly enabling them to compete with fossil fuel-derived plastics.

Other biopolymers that have been combined with nanoclays include chitosan, starch, casein, whey and gelatine (Marsh and Bugusu, 2007). Soy protein has also seen increased interest because of its biodegradable characteristics and thermoplastic properties. Limitations include brittleness and poor moisture barrier properties which can be overcome by adding plasticisers and reinforcers. The potential applications vary from stand-alone barrier films, to coatings on other polymers and paper-based packaging, to direct coating of foodstuffs.

Such biodegradable nanocomposites could be of use in other agri-food application areas, such as on-site farm use (e.g. wrappings for feed and hay that are currently either sent for landfill or incinerated by farmers), estimated to be around 6.5 million tonnes per annum (Robertson, 2006). Instead of incineration, they could be composted and returned to the soil.

Bio-based nanofibres

Another approach using nanotechnology is the processing of pure bioplastics into nano threads or fibres that can be woven into a material. This is a convergence of nanoprocessing technologies and bio-based polymer production. A number of biopolymers including chitosan, cellulose, collagen and zein (made from corn) have been synthesised as nanofibres via electrospinning (Ramakrishna et al., 2006). In some cases, these have superior properties to traditionally cast polymers, including increased heat resistance.

In addition, mats of such nanofibres possess a highly nanoporous structure and can be used as support matrices for other materials or substances in multifunctional materials. Corn-sourced zein is a promising biopolymer for packaging due to its strong water resistance properties. Zein also has good mechanical properties in nanofibre-form when produced via electrospinning (Torres-Giner et al., 2008).

One of the most interesting materials is created by electrospinning blends of zein and chitosan (de Azeredo, 2009). These blends are reported to have great potential for application in active and bioactive packaging, antimicrobial and anti-fungal food coatings, and in the biomedical and pharmaceutical areas. However, at the time of writing, chitosan still needs regulatory approval as a food contact material.[8]

Edible films and coatings

The third nano-bioplastic innovation harnesses the novel properties of bio-based materials to create edible and biodegradable films that prolong shelf life, improve packaging characteristics and reduce packaging waste. These films are layers of digestible material used to coat food (edible coatings) or to act as a barrier between food and other materials or environments (edible films). Food can be coated by being dipped into solution, by spraying or by application with brushes or sponges. Films are created separately and then applied via a food packaging system.

Sugars (such as chitosan and cellulose), proteins (such as zein and collagen) and fats (such as triglycerides and fatty acids) can be used as edible film-forming materials. Bionanocomposites created from vegetable and fruit puree and cellulose nanowhiskers have been described in a review by de Azeredo (2009). Proteins suitable for films and coatings include casein, whey, collagen, egg white and fish-derived protein. Soya bean, corn and wheat proteins can also be used to produce edible films.

However, harnessing these improved functionalities is complicated because of limitations such as poor barrier properties (gas and moisture permeability), brittleness and cost (Dalmas et al., 2007). There are considerable differences in the characteristics of biopolymers used for edible films and coatings. For instance, polysaccharide films are low cost but exhibit low moisture-barrier properties. Protein films have functional properties such as good plasticity and elasticity as well as good oxygen barrier properties, but poor water barrier properties. Lipid films have good moisture barrier properties, but poor oxygen barrier and mechanical properties.

Research and development of bionanocomposites for edible film applications is expected to grow in the next 10 years and the application of bionanocomposites promises to expand the use of edible and biodegradable films in the agrifood sector (Lagaron et al., 2005).

Product development and manufacturing

Product development and manufacturing of nano-bio materials for food-packaging are beginning to emerge, although there are currently few stable supply chains for such advanced materials. Scale-up in certain processes will mean that some of the new and improved materials described above should be

available in significant quantities within the next 2-5 years, sooner if there are radical developments in the area.

For example, Innovia films has developed and patented a compostable nanoparticle-coated foodstuff packaging with improved gas barrier properties using nanoparticles of starch and synthetic polymers.[9] Other nanoclay-polymer nanocomposite barrier products have been reported to be commercially available (Greiner, 2009) such as: NycoNanoTM (NYCOA, United States); NanoblendTM (PolyOne, United States); NanomideTM (Nanopolymer Composites Corporation, Taiwan); Systemer (Showa Denko, Japan); and Ecobesta® (Ube Industries Ltd, Japan).

Robinson and Salejova (2010) reported that some companies (such as Nanograde GmbH) market polymer composites containing nanoparticles of silver and calcium phosphate that demonstrate microbicidal activity. Some companies are also including nanoparticles in food container products, including Sharper Image® (United States), A-DO Global (China), BlueMoonGoods (United States), Everin (United Kingdom) and JR Nanotech Plc (United Kingdom).

Capturing the value of promising knowledge from research and development relies on financial and managerial support, whether in a large firm for a new development line, or supporting a techno-starter/spin-off.

A key challenge for these emerging supply chains is to successfully link up nanotechnology developments with food packaging chains. Funding is required to support scale up and is being sought from limited venture capital funds, which are often risk averse. Scale up could also be supported by large firms present in the supply chain, wanting to benefit from the advances in materials, again with inherent risks related to proof of the sustainability of the material within the context of full-scale manufacturing and distribution. In the case of nanobiomaterials, it needs to be demonstrated that large amounts of a new material can be provided with consistent quality in order to compete with established providers. Attracting investment for radically new materials requires convincing the packaging firms that consistent large-scale quality can be achieved, which means new entrants have to carefully consider their expansion strategy and show the capability to scale up on demand.

One success story in Europe is Nanobiomatters, a medium-sized firm based in the greater Valencia region. Over the past six years, Nanobiomatters has developed R&D and production capabilities for nanoclay powder production (Commercial Additive Plant of 2500t/year) and polymer-clay nanocomposite production (Commercial Extrusion Plant of 4000t/year). Nanobiomatters is rapidly becoming a significant company in the field of biodegradable materials for food, medical and pharmaceutical sectors with commercial products currently available and with EUR 4 million invested in its manufacturing facilities. It also has a diverse portfolio of nanobioplastics (including antimicrobial and gas scavenging functionalities).

However, research into the activities of Nanobiomatters from 2008 onwards (Robinson and Propp, 2011) shows that it relied on multiple product families of different degrees of complexity. A strategy of choosing a relatively lower-performance product line, compared to other innovative materials in their portfolio, was used to build up production capabilities for various materials, to develop standards and protocols, to garner interest from investments and build a stable business.

Impacts on society, public debate and governance

Public Debate

Government-led engagement exercises aimed at anticipating and addressing public concerns have increased in recent years. There have been a number of national initiatives in this area. In addition, the

OECD Working Party on Nanotechnology has considered issues surrounding engagement on public interest in nanotechnology and in order to assist policy-makers and implementers in this area has produced a "Planning Guide for Public Engagement and Outreach in Nanotechnology" (OECD, 2012).

In this context, nanotechnologies for use in the food and packaging sector have stimulated much debate in the past decade. Interaction between consumers and the food sector began in the early 2000s in response to growing concerns of nanotoxicity coupled with rapid development in this sector. A number of nano-engagement exercises were initiated.

For example, the IG DHS professional association of Swiss Retailers[10] explored the regulation gap in nano and the food sector, as well as issues of consumer confidence. They developed a code of conduct with the assistance of the Innovation Society (a risk management consultancy), published in 2008 (IGDHS, 2008). There have also been calls for nanotechnology moratoria (for example, from ETC group),[11] and the British Soil Association[12] has argued that specific values and codes must be considered to inform the organic food production debate.

The British Food Standards Agency published a report of consumers' views on the use of nanotechnology in food and food packaging (Food Standards Agency, 2011), using focus groups in the United Kingdom to explore attitudes towards a number of nano-applications in the food sector. In a study of public attitudes towards nanotechnology in Switzerland reported by Siegrist et al., (2008) and by Burri and Belluci (2008), the public position was described as pragmatic, with a focus on information transparency and a preference towards nano in food packaging when compared with other nanofood applications.

What is clear is that consumer perspectives are, and will continue to be, important in the commercial development of nanotechnology converged with biotechnology as applied to the food sector. Engagement exercises stimulated by public agencies and other organisations are an important part of the nanofood landscape and the form and function of these interactions will play a strong role in the emergence and societal embedding/rejection of nanofood options.

Currently food packaging is discussed alongside other parts of the food sector and because of the use of the umbrella term of nanofood, packaging is often involved in debates which include food fortification with nano nutrients, nanosensors for food production and nano-related agrochemical R&D.

To take public engagement of converging technologies forward requires a focus on application areas (healthcare, food, lifestyle etc.), though a clear link between public involvement and actual design/development of converging technologies must be visible if trust is to be achieved.

The labelling debate

Another challenge for nanobiomaterials in the packaging sector is the regulatory environment, specifically as it relates to four elements: food-contact materials; use of plastics;[13] consumer law (labelling); and nanotechnology specific guidance. Innovation, production and deployment of the options outlined above require the alignment and stabilisation of these four elements. Work by the OECD on the "Regulatory Frameworks for Nanotechnology in Foods and Medical Products: Summary Results of a Survey Activity" (OECD, 2013) provides an overview of country activity in this area.

Specific to nanotechnologies, EFSA[14] set up an expert working group for nanotechnology applications in 2007[15] involving people from national food safety authorities. The group launched (in early 2008) a "Call for Scientific Data on Applications of Nanotechnology and Nanomaterials used in Food and Feed" (EFSA, 2008) with a focus on information related to risk assessment procedures for nanomaterials.

Following this initiative, EFSA published first a draft and then, in February 2009, a final scientific opinion on the potential risks from the application of nanotechnologies as related to food and feed safety and the environment (EFSA, 2009). The view was that the use in Europe of nanotechnology for food applications was in principle sufficiently regulated by Regulation EC/1935/2004[16] that covers all materials coming into contact with foodstuffs.[17]

The issues posed by the possible introduction of a labelling scheme related to food products that contain nano-materials are multi-faceted. At a conference in June 2009 organised by the Transatlantic Consumer Dialogue (TACD), a forum of 80 European and US consumer organisations, there was a clear indication that there should be labelling of nanotechnology in foods. With the lack of specific nanotechnology regulation, they argue that the consumer must have the opportunity to choose between food products involving nanotechnology and other options. The amount of information on the label, the degree to which consumers can interpret the data and the specificity of the information are additional issues that must be resolved, otherwise nanotechnology enabled products may be unfairly singled out and misrepresented. They went on to argue that what is needed is a labelling system that allows consumers to make an informed choice.

Understanding the role and impact of such a scheme is important. Throne-Holst et al. (2011) argued that labelling in itself is not straightforward as there are issues of distribution of responsibility. For example, the consumer/citizen has the responsibility to make a choice on whether to buy a product incorporating nanomaterials, but evidence shows that there is a low level of knowledge about nanotechnology in the general public. There have been many studies of the public perception of nanotechnology, and there is data that public awareness of nanotechnology is limited at best (Waldron et al., 2006; Gaskell et al., 2005;, Cobb and Macoubrie, 2004). Thus it is difficult to predict how consumers will react to labelling.

It is clear that regulation of such converged nano/bio innovations is complex and, from the examples above (drawn from the European context), there are considerable practical issues to consider in this area.

Key observations

Even in this focused domain of food packaging there are:

- A variety of potential applications.
- A number of waste management solutions (biodegrading in the current waste system, dedicated composting or eating the packaging).
- Challenges in the scale-up of bionanomaterial supply chains, including the development of standards and a clear regulatory framework.
- Issues for engagement, including the (often confusing) use of umbrella-labels such as Nanofood, to encompass technologies with different benefits and potential risks (c.f. food packaging versus food fortification), but also different user cultures related to them.

Nano-convergence for targeted drug delivery

This example presents drug delivery as an area of application of technology convergence. Of interest in this case is that convergence is occurring in laboratories, through interdisciplinary science, and also at the industrial level, where new drug delivery technologies are being utilised in the biotechnology and

pharmaceutical industry. In this example, some quantitative studies of the web-of-science are used to illustrate issues related to the growth of the field

Overall policy driver: The promise (why people are interested)

Nano-convergence in the health sector (nanomedicine) is an area of much promise in terms of the delivery of new and improved healthcare provision. However, the intersection of various actors in nanomedicine – be they pharmaceutical companies, manufacturers or patients – is complex, and likely to lead to challenges in innovation and uptake. Uncertainties in terms of risk, acceptance by patients (public) and the scope of future developments in nanomedicine means that companies and manufacturers of nanomedical products tend to be cautious or prefer to wait for market and regulatory stabilisation.

This section focuses on drug delivery as one of many nanotechnology applications in this sector which show signs of technology convergence. It is particularly illustrative due to the fact that involvement of nanotechnology can occur in a variety of ways, as part of a drug delivery system in conjunction with other technologies, or integrated from the very start into a therapeutic-plus-drug delivery combination. The field of nano-involved drug delivery is vast and the following sub-sections are not exhaustive, but provide evidence for some conclusions about technology convergence in this sector.

Scientific research

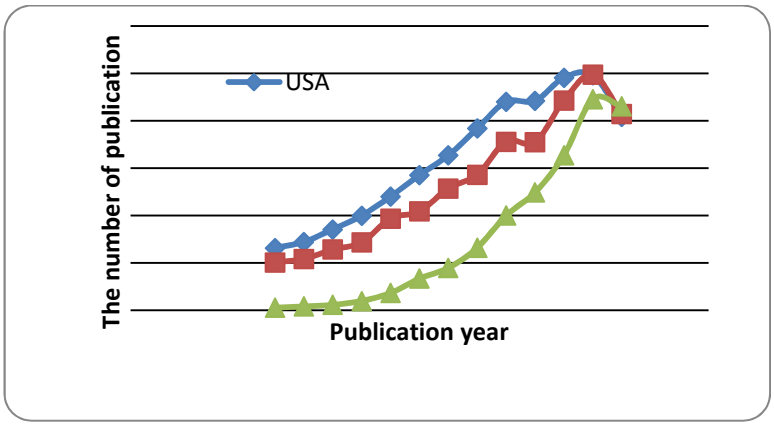
The field of drug delivery is developing rapidly and has the attention of scientists, pharmaceutical researchers and industry alike (Boyd 2008). The development of delivery systems that transport and deliver a drug safely and precisely to its site of action is now a key focus. Indeed, a large number of new delivery technologies are developed each year and nearly every part of the body has been studied as a potential route for administering both classical and novel medicines.

Consequently, promises of new ways of delivering poorly-soluble drugs, peptides and proteins are attracting a great deal of attention. One of many possibilities is nanoparticle-enabled drug delivery and targeting. In addition, alternative drug delivery technologies using nanotechnology are currently under intensive study (transdermal patches, nanodevices, bioadhesive systems, implants, microfabricated systems, cell encapsulation devices and novel nasal drug delivery systems) (Kim et al., 2009).

Research in nanotechnology-enabled drug delivery (NEDD) is diverse, expanding and accelerating, with some of the most active areas including: polymer conjugates, nanogels, dendrimers, liposomes, micelles, lipid nanoparticles, nanoemulsions, polysaccharide nanoparticles (such as chitosan), magnetic nanoparticles, ceramic nanoparticles, nanoshells, cyclodextrin nanosponges and nanocrystals (Zhou et al. 2013).

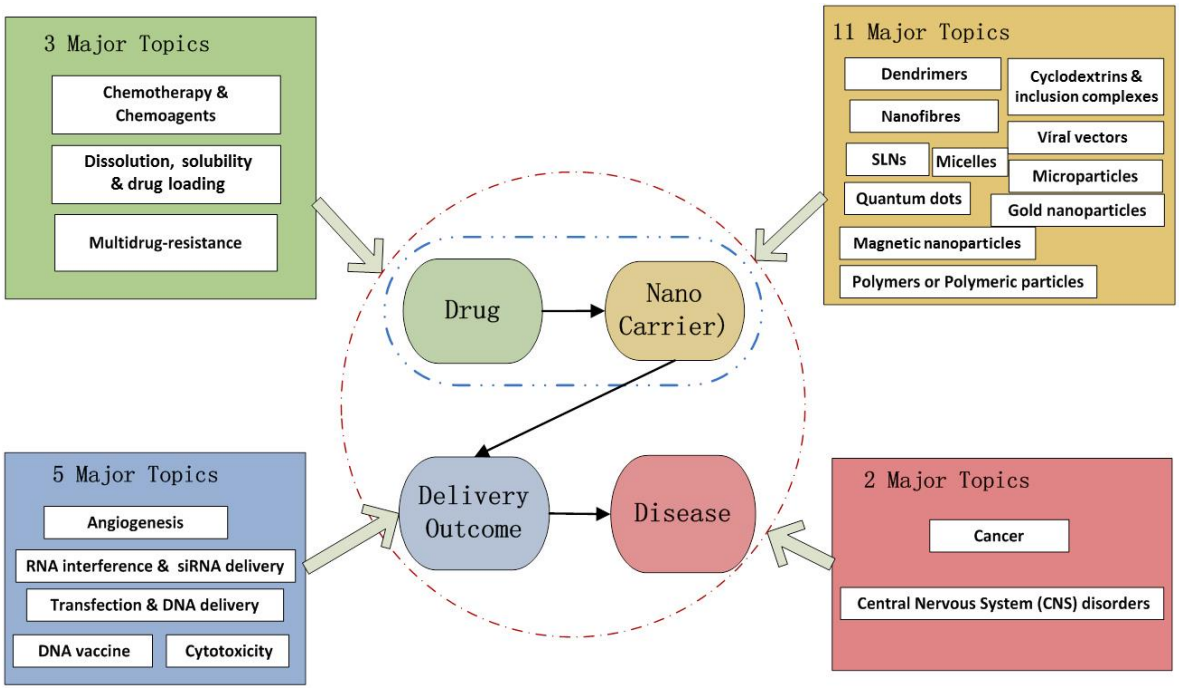
In a recent study, the number of publications related to nano-enabled drug delivery was shown to be growing steadily and in a similar way across three representative countries or regions: China, the United States and the European Union[18] (Figure 1).

Figure 1. The total publication trends for China, United States and European Union



Source: Adapted from Zhou, X., A.L. Porter, D. K. R. Robinson and Y. Guo, (2013), 'Analyzing Research Publication Patterns to Gauge Future Innovation Pathways for Nano-Enabled Drug Delivery' PICMET '13 Conference. "Technology Management in the IT-Driven Services" 28 July – 1 August, 2013: Portland, United States.

Figure 2. Simple schematic of a nano-enabled drug delivery system



Source: Adapted from Zhou, X., A.L. Porter, D. K. R. Robinson and Y. Guo, (2013), 'Analyzing Research Publication Patterns to Gauge Future Innovation Pathways for Nano-Enabled Drug Delivery' PICMET '13 Conference. "Technology Management in the IT-Driven Services" 28 July – 1 August, 2013: Portland, United States.

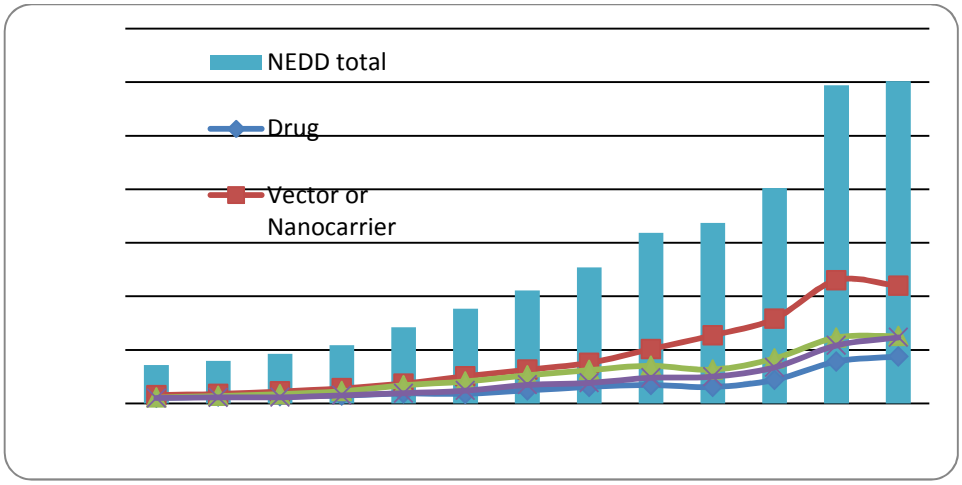
The first subsystem, *drugs* (or genes or other active agents), can be considered as the cargo of the Nano-Enabled Drug Delivery (NEDD) system (a simple schematic of which is shown in Figure 2). As the first part of the whole system, drugs link with the other three subsystems. Three major topics are associated with the drug subsystem: chemotherapy and chemoagents; dissolution, solubility and drug loading; and

multidrug-resistance. Chemotherapy and chemoagents account for over 70% of the drug subsystem publications (reflecting a focus on cancer therapy).

The second subsystem of *nanocarriers* accounts for half of the NEDD search set. This reflects the search algorithm used, keying on "nano-enabled" to distinguish from traditional drug delivery endeavours. Some areas, such as gold nanoparticles, magnetic nanoparticles and polymers, show a rapid increase in research activity.

The other two subsystems, **disease** and **delivery outcomes**, share similar developmental trends. Publication rates were low until 2007, at which time an increasingly sharp rate of publication is identified. Topics involving "delivery" - particularly, RNAi (include siRNA delivery) and transfection and DNA delivery – are developing fast. In the disease subsystem, cancer therapy is the most common aim (some 9 666 of the 61 465 WoS records), despite the search not directly incorporating cancer-related terms. Trends for the four subsystems are shown in Figure 3.

Figure 3. Research Publication Trends for each NEDD Subsystem (WoS)



Source: Adapted from Zhou, X., A.L. Porter, D. K. R. Robinson and Y. Guo, (2013), 'Analyzing Research Publication Patterns to Gauge Future Innovation Pathways for Nano-Enabled Drug Delivery' PICMET '13 Conference. "Technology Management in the IT-Driven Services" 28 July – 1 August, 2013: Portland, United States.

Table 1. Relationship between major topics and subsystems showing the number of hits in the WoS database for NEDD.

	Subsystem records	**7442**	**20541**	**13065**	**9945**
Topic hits	*Major Topic \ Subsystem*	*Drug*	*Nanocarrier*	*Delivery Outcome*	*Disease*
9666	Cancer	29.0%	26.4%	26.1%	100.0%
6990	Polymers	11.6%	100.0%	26.1%	11.0%
5242	Chemotherapy & Chemoagents	100.0%	20.9%	20.5%	45.8%
4931	RNA interference and siRNA delivery	5.4%	17.4%	100.0%	24.1%
3969	Transfection and DNA delivery	2.4%	51.1%	100.0%	8.5%
3321	Cytotoxicity	25.6%	35.3%	100.0%	24.2%
2921	Viral vectors	1.6%	100.0%	25.7%	10.0%
2670	Microparticles	12.1%	100.0%	14.1%	7.2%
2588	Magnetic nanoparticles	8.8%	100.0%	13.8%	23.4%
1911	Micelles	17.4%	100.0%	9.5%	13.8%
1755	Dendrimers	7.6%	100.0%	28.1%	13.2%
1703	Gold nanoparticles	6.3%	100.0%	18.6%	20.8%
1599	Dissolution, solubility and drug loading	100.0%	45.7%	5.9%	7.5%
1334	Quantum dots	3.9%	100.0%	17.9%	22.1%
1306	Angiogenesis	9.8%	24.0%	100.0%	34.2%
1272	DNA vaccine	2.8%	30.1%	100.0%	12.7%
1243	SLNs (solid lipid nanoparticles)	20.6%	100.0%	11.7%	14.6%
1235	Multidrug-resistance	100.0%	21.4%	20.0%	51.8%
1177	Nanofibres	3.1%	100.0%	7.3%	2.4%
693	Cyclodextrins and inclusion complexes	16.2%	100.0%	13.0%	7.1%
294	CNS disorders	6.1%	28.2%	21.4%	100.0%

Source: Adapted from Zhou, X., A.L. Porter, D. K. R. Robinson and Y. Guo, (2013), 'Analyzing Research Publication Patterns to Gauge Future Innovation Pathways for Nano-Enabled Drug Delivery' PICMET '13 Conference. "Technology Management in the IT-Driven Services" 28 July – 1 August, 2013: Portland, United States.

Each of the 21 topics in Table 1 (which originate from Figure 3) is closely linked with one subsystem, but is usually also strongly related to others. Chemotherapy has a strong linkage with the disease subsystem, which is not surprising given that half of the disease publications relate to cancer, of which chemotherapy is the most effective treatment. Another important cancer related topic is multidrug resistance. Half of these publications link to cancer therapy (for example, research on 2-Methoxyestradiol to overcome drug resistance in multiple myeloma cells). As an aside, it is worth noting that there are several research centres especially active in this area (University of Texas, National University of Singapore, and Northeastern University).

In addition, half of the publications in Transfection and DNA delivery focus on nanocarriers (as gene delivery, e.g. DNA and RNA, is inherently nanoscale) and it is noted that attention to cytotoxicity in delivery has recently drawn increasing attention, with 35% of the publications in cytotoxicity related to the nanocarrier subsystem. NEDD is a strongly connected system with each subsystem strongly connecting to

the others, and likewise for major topics. Understanding the degree of connection amongst the subsystems and major topics can aid research management in terms of supporting relationships between activities.

Product development and manufacturing

As noted above, the development of next generation advanced multifunctional drug delivery systems has become a key focus for researchers. Also, it is in the development of delivery systems that are targeted, traceable, have limited negative effects and can control the release of the drug, where a further level of convergence is seen.

For some regions of the body, issues of transport have become significant and consequently new methods of delivery are being demanded. For example, getting a drug into the cytoplasm of a living cell within the human body has many challenges e.g. avoiding processes such as kidney filtration. Such properties have recently been termed "stealth characteristics".

In Europe, there are a large number of projects investigating converging nanotechnologies for drug delivery applications. For example, from the European Research Area Network for Nanomedicine (EuroNanoMed), projects include: Nano4Neuro, in which nano-functionalised implants for the regenerative treatment of spinal cord and nerve lesions are being investigated; DENPEPTHIV, in which peptide-associated dendrimers are being explored in dendritic cells for the development of new nano-HIV vaccines; and NANOSTEM, to create a combined therapeutic platform for cancer stem cells.

One important aspect of nanotechnology-based drug delivery systems is that they cannot be developed in total isolation in a research laboratory, needing to link up with those developing the drug to ensure conjugation (the binding of the medicine to the delivery system). This requires knowledge of the pharmacokinetics of the drugs (i.e. where the drug goes and what it reacts with) as well as knowledge of the disease/disorder to maximise targeting efficiency and minimise toxic effects.

The emerging move away from generic drug delivery to a variety of multifunctional disease- or region-specific drug-delivery systems is a move towards the development of nano-enabled systems. The changing shape of the pharmaceutical value chain to include a variety of applications of nanotechnologies and biotechnologies (often supported by sensor and imaging technologies) means new types of innovation alliances and perhaps new business models are developing.

A variety of companies are entering clinical trials such as Magforce (based in Berlin) and Nanobiotix (based in Paris) both targeting cancer, with the candidate nanodelivery system being developed alongside the drug candidate. Figure 4 shows some examples of drugs that are in clinical trials with nanotechnology-enabled delivery systems.

In the past eight years, a number of co-ordinating forums have emerged that are attempting to align actors to create value chains. They are operating in an area of high uncertainty with respect to the technology and the diversity of its forms and applications. Looking at Europe, one platform is the European Technology Platform for Nanomedicine, a public research and private R&D network that determines strategic agendas (formalised expectations of the community) and creates roadmaps.

However, interaction of the public and private R&D sectors with the potential users of the nanomedicines has been less visible. A focus on the users has been the aim of CLINAM,[19] an annual conference at which the medical community (doctors and medical researchers) congregate to explore the most advanced nanomedicine-related research and to speculate about potential and desirable futures. Further, NanoBioRAISE (Schuurbiers et al. 2007) was a European project aimed at articulating potential governance and ethical challenges for nanomedicine, in order to provide intelligence for both governance actors and innovation actors alike.

Figure 4. Drugs in clinical trials using nanotechnology as part of the delivery system

Vector Family	Examples
Liposomes	
Liposomes	Amphotericin B, Daunorubicin , Doxorubicin
Micelles	
Phospholipid	Paclitaxel, Camptothecin, Diazepam
PluronicR	Doxorubicin (SP1049C), Preclinical Paclitaxel, Tamoxifen, Etoposide
	Doxorubicin (NK911), Antisense oligonucleotides
	Polyester Paclitaxel, Doxorubicin,
Nanoemulsions	Amphotericin B, Paclitaxel, Dexamethasone, Benzathine penicillin G
Nanoparticulate systems	
Drug nanocrystals	Amphotericin B, Etoposide, camptothecin, paclitaxel
Polymer -based	Tamoxifen, Cyclosporin-A, Theophylline,
Lipid-based	Doxoribicin, Camptothecin
Ceramic-based	2-devinyl-2-(1-hexyloxyethyl)pyropheophorbide
Albumin-based	Paclitaxel, DNA and antisense, oligonucleotides
Nanogels	Oligonucleotides
Dendrimers	Indometacin, 5-fluorouracil, Antisense oligonucleotides

Source: Adapted from Robinson, D. K. R., A. Porter and Y. Guo, (2012), "Vector platforms for nano-enhanced drug delivery: capturing innovation pathways in the making" Paper presentation at the International Conference on Innovative Methods for Innovation Management and Policy, Beijing, May 2012.

Looking at the whole value chain, MEDITRANS (see Parandian et al., 2012) focuses on translating R&D on nanotechnology into medical value chains. Comprised of a diverse set of firms (including large pharmaceutical firms) they assess expectations and the project innovation pathways that are the most promising. These can act as a guide to align value chains. Other similar activities, such as strategy articulation workshops, have been incorporated in R&D consortia for Nanomedicine.

The Nanomed Round Table project was organised to provide European stakeholders with a set of recommendations to support decision making regarding nanomedical innovations. For example, the Sixth European Framework Programme network of excellence for nano and the life sciences (FRONTIERS) included Constructive Technology Assessment projects to explore potential configurations of actors in terms of value chains, governance and actors roles and activities (Robinson and Propp, 2008).

These examples indicate that, to be able to align value chains in nanomedicine, R&D actors are creating forums to articulate potential futures and are using these as scenarios in evaluating the likely technological and innovation challenges, as well as societal and governance issues, in order to develop optimal routes from the laboratory bench to the bedside. Unlike the previous case study of sustainable and green packaging, nanomedicine appears to have a relatively coherent community and industrial structure related to the production and application of healthcare technologies.

Impacts on society, public debate and governance

Societal attitudes to health can lead to a higher tolerance of risk in terms of novel therapies such as drug delivery techniques, as opposed to innovations in other sectors in which risk may be perceived to outweigh benefits. In this section, discussion focuses on regulation and examines where nanomedicine (as

a broad field of technology convergence of which drug delivery is a part) is governed by a number of complex existing regulatory structures.

Multiple regulatory environments: Example of nanomedicine

While it is anticipated that nanomedicine innovation will radically change the healthcare sector, it is also expected to challenge existing perceptions, dynamics and standards relating to ethics, patient and environmental safety, and governance (D'Silva and Bowman, 2011).[20] Most studies of nanotechnology governance look at the enabling nanotechnologies themselves (mostly nanomaterials) to explore the risks, regulations and standards for nanomaterials.

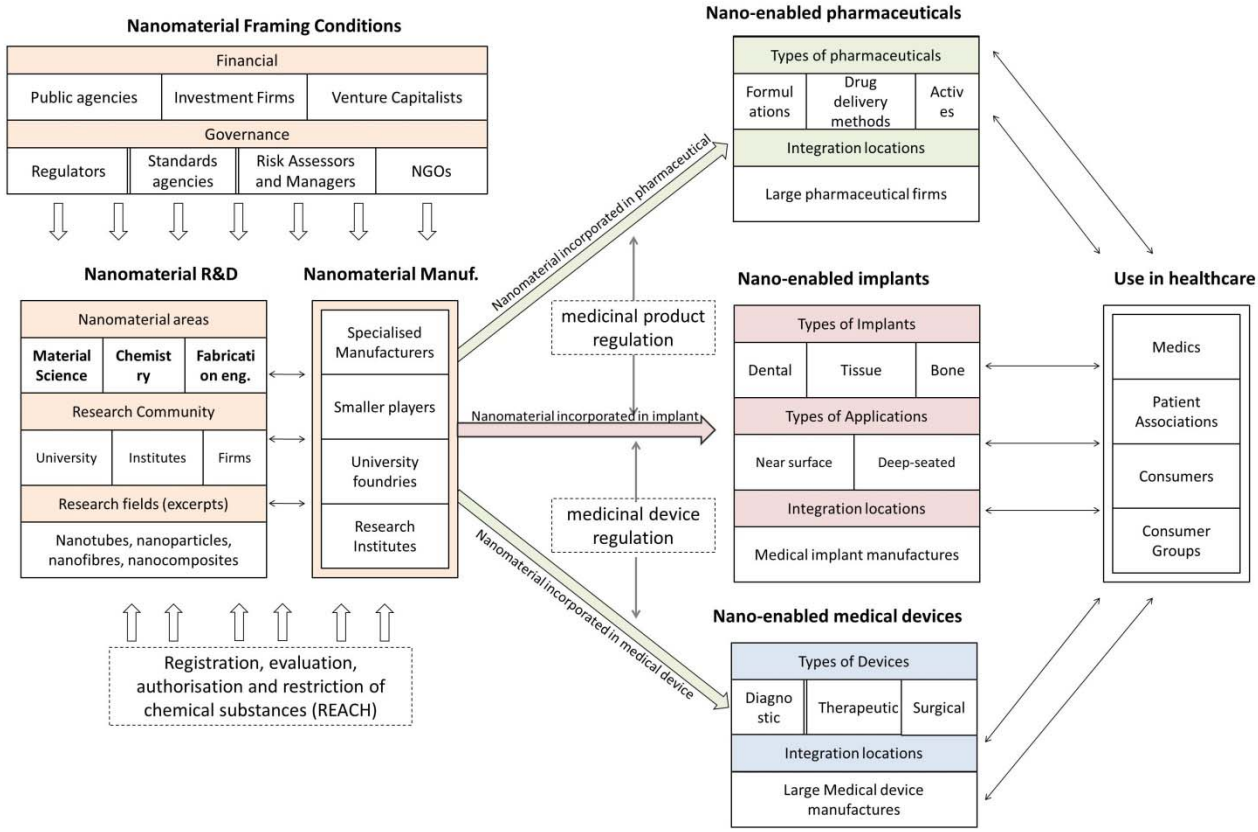
For converging nanotechnologies, another approach is to look at the potential application envisioned in the future and to speculate on the governance arrangements that will be needed to mitigate the risks and gain the benefits. Such consideration in areas such as nanomedicine (for example, drug delivery) is important if anticipatory forms of regulation (the opposite of wait and watch regulatory strategies) are to be applied.

Studies of innovation show that there is a translation of promising technologies into products in society. The translation occurs at the level of industries in particular sectors. It is often stabilised configurations of actors that act to add value in the conversion of an original technology into a workable device/product.

In Figure 5 below, the key activities in the creation and embedding of converging technologies for healthcare involving nanotechnologies are charted. On the left is the production of knowledge, new materials in laboratories and the manufacturing/product development stage where the converged nanotechnology is transformed into a product. Alongside the regulatory environment of nanomaterial manufacture, each of the three product development pathways has an evolving regulatory environment not designed for situations of converging technologies.

The boundaries between medicinal products, devices and therapies are likely to become blurred as advances continue to be made in this application area. The convergence between these is commonly referred to as "borderline products" and to date the most frequent borderline products have occurred between medical devices and medicinal products. In order to determine whether a product is a device or a medicine, the definitions of both need to be considered, along with the claims for the product, the mode of action on the human body and the intended purpose of the product (D'Silva and Van Calster, 2010).

Figure 5. Nanomaterial supply chains feed into three broad medical innovation chains: Pharmaceuticals, implants and medical devices



Source: Adapted from Robinson, D. K. R. and A. Rip, (2012), "Socio-economic Dynamics of Innovation and Uptake" Joint OECD/NNI International Symposium on Assessing the Economic Impact of Nanotechnology, Washington. March 27- 28.

Depending on the classification, regulatory requirements for pre-market and/or post-market processes are applied, with variation in the regulatory pathways existing for medical devices, medical products or therapies. For example, the European Medical Device Directive,[21] was developed and adopted on the premise that the Directive shall not be applicable to *in vitro* diagnostics.

Several harmonised standards have been designed for certain types of device, as in the case of standards for *in vitro* devices. If applied to devices that are not *in vitro* devices, legal conformity cannot be assumed. It can also be argued that the blurring of traditional boundaries has the potential to challenge the competencies of notified bodies charged with the responsibility of assessing and authorising borderline products.

One key area in which nanotechnology convergence is promising potential transformational changes is personalised medicine. Multiple drug delivery platforms are a potential contributor to a shift from generic drugs to personalised therapies. Also, if one looks at synthetic biology (another area of converging technology), drugs are expected to be synthesised in future (Carothers et al., 2009) through synthetic biology techniques, which may result in challenges for regulators and those aiming to adhere to regulations. Since the regulatory framework for synthetic biology is still in development, it could be reasonably expected that drug manufacture using a converged nano technique (synthetic biology) would fall under the genetically modified organisms (GMO) regulatory frameworks. This has consequences, since it then links up with the current approaches to GMO governance.

Key observations

Nano-enabled drug delivery integrates a number of different elements into a therapy in an example of the convergence of:

- Disciplines in the development of nanocarriers (for example, materials science, molecular biology and pharmaceutical science); and
- Industry structures (for example, integration of nanoscience within the biotechnology and pharmaceutical industries).

The complexity of the convergence requires a large amount of co-ordination and collective discussion to allow priority setting and the development of technology and industry roadmaps. A key issue here, and more broadly for nanomedicine, is regulation. As many of the nano-enabled drug delivery examples described in this section may fall under different regulatory regimes, this may pose a serious challenge for product development in this area.

Neurotechnologies for health and well-being

This example examines the growing demand for developments based on neurotechnologies, but also highlights a disconnection between actors in the value chain. At the level of research, activities focus on improving the performance of neuron-silicon interfacing, utilising nanotechnologies in a variety of ways, whereas industrial application remains focused on the incremental evolution of relatively low performance technologies. Also, public engagement and societal reflection in this area of converging technologies seems only partially to reflect actual activities in the laboratory or the firm, focusing instead on the NBIC visions of human enhancement.

Overall policy driver: The promise (why people are interested)

Neurotechnologies have been part of the NBIC and Converging Technology visions since the early 2000s. The promise of augmenting human cognitive functions, both for purposes of human enhancement and for therapeutic applications such as advanced prosthetic limbs (Roco and Bainbridge, 2002), was central to discussions of NBIC (Ferrari et al., 2012).

Neurotechnologies currently form only a small portion of the healthcare market, though the market has grown (van Est and Stemerding, 2012), possibly reflecting the limited efficacy of drugs for neurological disorders (e.g. for Alzheimer's disease and epilepsy). Miller (2010) provides evidence that a number of major pharmaceutical firms are shifting their investments away from psychopharmaceuticals towards neurotechnologies. He provides the example of Pfizer's investment in Neuronetics, a neurotechnology firm based in the United States (Miller, 2010).[22]

Alongside this suggested shift from psychopharmaceuticals to neurotechnologies is an increase in demand related to the ageing population (where neurological disorders prevail), an increasing understanding of brain function, and improvements in detection and diagnosis of psychiatric disorders (van Est and Stemerding, 2012), all of which are driving development.

Scientific research

Neuro-electronic interfacing has been emerging since the early 1990s with the pioneering work of Peter Fromherz, who interfaced living nerve cells to integrated circuits. Nerve cells, or neurons, communicate via electric potential, similar to electrical circuits: hence, the idea of using electric potential as a means of communication between a living cell and a machine.

An early nerve cell interface experiment was presented in the peer-reviewed scientific journal *Science* (Fromherz et al., 1991). Since this early work, a field of neuron-silicon interfacing has emerged which focuses on improved and sustained communication between the machine element (the integrated circuit and probe) and the living element (a nerve cell or whole slices of the brain).

Neuro-electronic interfacing was brought to the fore when Kevin Warwick of Reading University, United Kingdom, became the first human to have a computer chip implanted into the nerves of his forearm so that he could control through the internet a remote robotic hand situated elsewhere (a demonstration of bio-, info- and cogno-sciences). He presents this experimentation as an "upgrade" to his human body.[23]

The ethical considerations here range from implants to improve the life of the physically and mentally disabled, through to ideas of upgrading the human body and increasing performance.[24] However, much of the discussion still lies firmly in the future, anticipating what will be the situation if such human enhancements proliferate.

The more global trend in R&D has been to grow and sustain living nerve cells on arrays of probes so that multiple connections to neurons and brain slices can be achieved, which is where nanotechnology plays a particularly strong role. Surface functionalisation of silicon arrays to be biocompatible with the nerve cells, and to keep the nerve cells in place (they have a tendency to migrate across surfaces), is a key challenge for the nano-surface of the array. Also the probes themselves are sub-micron, thus nanofabrication techniques are necessary.

However, it is clear that there has been little or no commercial application of nano-related neurotechnologies to date, as discussed below.

Product development and manufacturing

One area in which relatively low performance neurotechnologies are already used is in stimulating specific areas deep within the brain for motor and psychiatric disorders. Deep brain stimulation (DBS), the implantation of stimulating electrodes in deep brain structures such as the subthalamic nucleus and globus pallidus, has emerged as a treatment for Parkinson's disease, essential tremor, and several other motor disorders over the past decades.

The field is still in its early stages, a niche application focusing on areas in which there are limited pharmaceutical-based options, but still has a reasonable amount of history to draw upon. Since the first successful thalamic DBS for Parkinson's (Limousin et al. 1998), to date over 50 000 patients have been implanted with deep brain stimulating electrodes.[25] DBS is perceived as having an advantage over surgical procedures (such as ablation and lesioning) and neuropharmaceuticals (which often have irreversible effects). Despite limited understanding of its mechanisms of action, DBS has proven effective for a number of movement and psychiatric disorders.

Despite currently being a niche application, DBS is seen by many to be on the verge of wider application, leading to interest from neurosurgeons, medical device manufacturers and regulators. DBS is under clinical investigation for a broad selection of neurological and psychiatric conditions, such as epilepsy, dystonia, Tourette's syndrome, depression, obsessive-compulsive disorder and cluster headaches (Robinson, Huang, Guo and Porter. 2013). Trials of an epilepsy neurodevice have also been undertaken by Medtronic Inc. with their SANTE device (Stimulation of the Anterior Nucleus of the Thalamus in Epilepsy) using DBS technology.

However, very little product development and manufacture is seen for convergence involving nanotechnology. This is curious, since there has been large investment in R&D in nano-related work on neuron-electronic interfacings. To explore this issue further, during the period 2008/2009, work began as

part of the Technology Assessment programme of the European Network of Excellence FRONTIERS[26] and in collaboration with IMEC.[27] The aim of this work was to explore the potential future development of deep-brain stimulation with a particular focus on nanotechnology.[28] Observing the lack of product development utilising nano-neurotechnologies, a research group leader in bio-electronics at IMEC wished to understand the possible pathways that would deliver innovative technologies (in-line with their institute objectives) and be optimised for uptake in healthcare practices.

A day-long workshop was conducted with neurosurgeons, medical device manufacturers, nanoscientists, technology transfer professionals and social scientists to explore the challenges facing nano-enabled innovations in DBS. Figure 6 shows some of the output. It is seen that, for each stage of development that a nano-enabled DBS would have to pass through, there were a number of challenges, for example in the niche testing at the level of neurosurgery.

One point emphasised is the existence of a "waiting game", in which large medical device manufacturers wait for breakthroughs from external research institutes and do not invest themselves. There is also a "technology push game", in which researchers and small spin-off firms push a technology in the research phase into the market.

On the side of the technology users i.e. the neurosurgeons, it was pointed out that improved technologies for surgery can mean that more resources (including time) are required within the healthcare system. Treatment cost analysis must include all aspects e.g. logistics during and after treatment. Education tools are also a serious bottleneck for new medical technologies, meaning device manufacturers must supply information and training. There is a mismatch between the nano-involved neurotechnology researchers, the medical device manufacturers and the neurosurgeons that is inhibiting the emergence of a clear value chain.

The example shows that, even for the basic steps in neurotechnology for deep-brain stimulation, there are issues of alignment up and down the value chain. These include trust by clinicians, availability of insurance coverage, logistics management, issues about the lifetime of the technology and the patient, the incorporation of new technology elements within the device, and the models and standards to allow consistent and safe products. For converging nanotechnologies these issues are compounded because of their multi-functional nature (they combine multiple characteristics from separate converging components).

Impacts on society, public debate and governance

Much of the early global[29] NBIC discussion focused on human enhancement through improving human performances, both individual and social (Roco and Bainbridge 2002). The healthcare promise of providing implants (such as deep-brain stimulators mentioned above), prosthetic limbs and artificial organs for medical applications was often combined with the idea of improving performance beyond that of a healthy human (Swierstra et al., 2009).

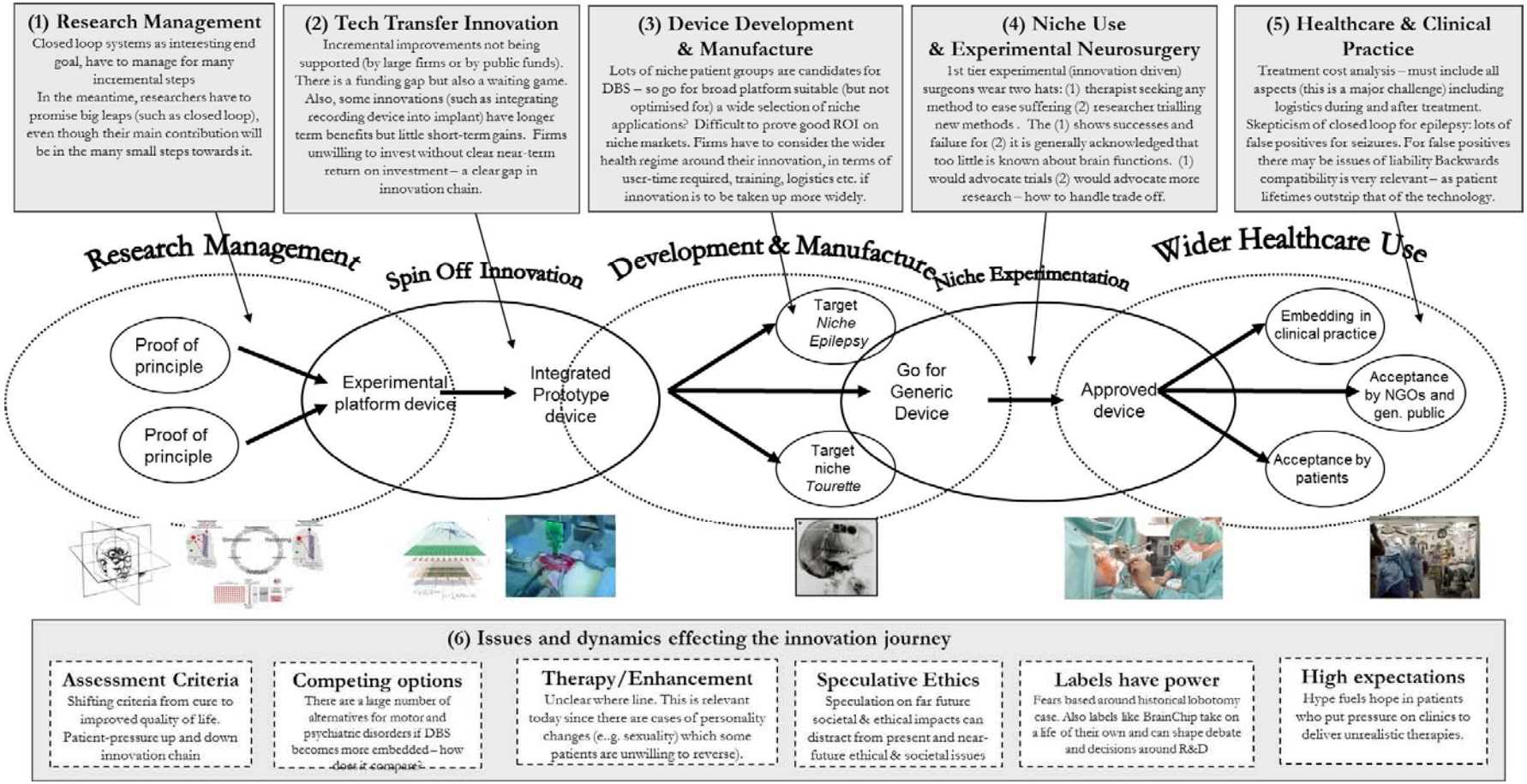
What is clear is that most of the debate from the early 2000s on ethical and societal consequences of converging technologies has focused predominantly on human enhancement, at the expense of questions more closely related to real current and likely future situations (Nordmann, 2004, Khushf, 2006, Grunwald, 2007 and Swierstra et al., 2009). Nordmann and Rip go so far as to make a plea for less speculative ethics.[30] They argue that there is a demand (a market) for ethics of new technologies and that ethicists, philosophers and social scientists have reacted with an over-supply of speculative ethics, which they define as follows:

> *"Speculative ethics leaps ahead in time. It focuses ethical concern on future worlds full of advanced materials, theranostics, smart dust for ambient intelligence, and human enhancement.*

> *"If-and-then' statements begin by suggesting possible technological developments and then indicate consequences that seem to demand immediate attention.*
>
> *What looks like a merely possible, and definitely speculative future in the first half of the sentence (the 'if '), turns into something inevitable in the second half (the 'then'). As the hypothetical gets displaced by a supposed actual, the imagined future overwhelms the present."* Nordmann and Rip (2009) p.273.

The promoters of speculative ethics frequently refer to a requirement that society (including researchers, policy makers, industrialists, etc.) must reflect on potential changes at an early stage, even if they are remote possibilities. Nordmann and Rip point out that there is a cost of raising irrelevant concerns, and that "there are good reasons to think that the opportunity costs of speculative ethics are too high, with less spectacular but more pressing 'here and now' ethical issues not getting the attention they deserve".

Figure 6. The development stages that a neurotechnology has to pass through from laboratory to clinic



Source: Adapted from Robinson, D. K. R., L. Huang, Y. Guo and A. L. Porter (2013), "Forecasting Innovation Pathways (FIP) for new and emerging science and technologies" Technology Forecasting and Social Change doi:10.1016/j.techfore.2011.06.004.

Nordmann and Rip do acknowledge, however, that the arguments for and against speculative ethics are coloured by the existence of the *Collingridge Dilemma*. This argues that while it is easier to change the course of a technology at its early stages, the way it will evolve is difficult to predict because of its early status. Conversely, at later stages, when a technology is well developed, it is difficult to change the form and function of that technology to suit different needs (the future is clearer, but the ability to change it is more difficult).

A middle ground has been suggested (Rip et al., 1995) in the form of controlled speculation of ethical and societal issues and consequences. The Dutch Nanotechnology Initiative (2005-2010) included a Technology Assessment programme (TA-NanoNed) to create tools to assist controlled speculation. A number of systems and approaches were developed to control speculation and to link up with actual dynamics. Constructive Technology Assessment (CTA), in which technology assessment is part of the construction of new science and technology fields, was the entrance point.[31] Different variations on this approach are seen elsewhere, both in the United States (Real-Time Technology Assessment) and Europe (Vision Assessment).[32]

Key observations

This example has noted the considerable activity on neurotechnologies related to convergence in natural science R&D, industrial product development, and social studies and humanities research. It is clear is that for each of these, the scope of (nano-involved) neurotechnology is different:

- For research scientists: it is about using nanotechnologies to improve performance in terms of neuro-electronic interfacing;
- For industry: the focus is on relatively low-performance neurotechnologies that can have a therapeutic effect, irrespective of the high-performance focus of researchers.
- At the level of social sciences: the focus of discussion and debate is on human enhancement related to the NBIC vision. It is thus highly speculative about the future, arguably at the expense of a focus current ethical concerns.

The different foci of actors at various points along innovation and value chains constitute a potential obstacle to the realisation of much of the early promise associated with the development of neurotechnologies.

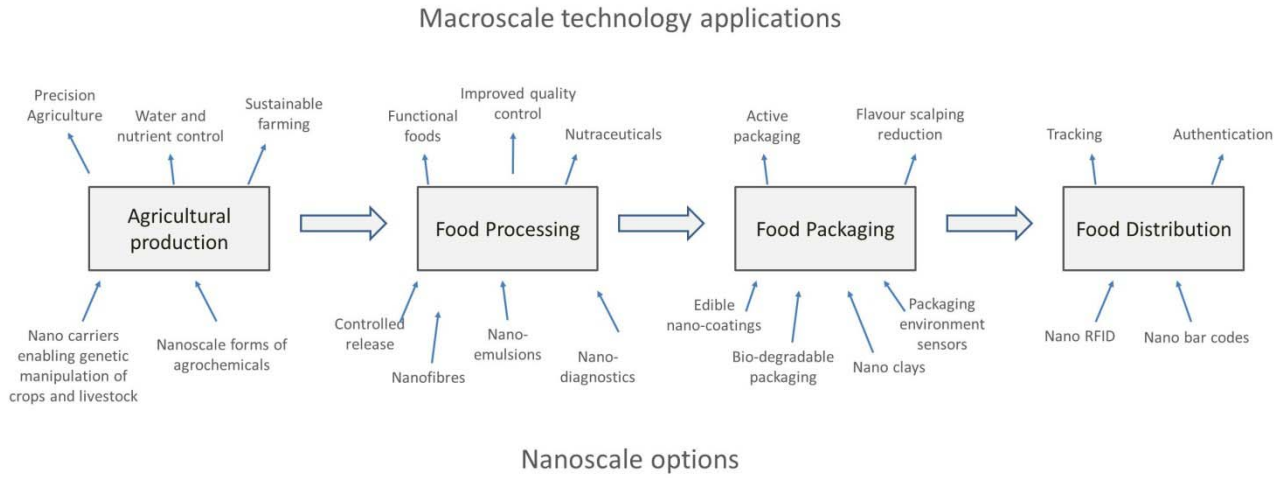
Food safety and security

This example demonstrates the large and diverse nature of research activity in sensor technologies stemming from nano-related technology convergence. It also highlights that there has been limited application of these technologies to date, with some exceptions in the food-processing and quality control areas. As a consequence, discussion of impacts on society, public debate and governance has been limited and is not covered in any detail. Rather, the example focuses on promising areas of sensor technology for the food sector and the challenges that may arise if and when product development activity increases.

Overall policy driver

Nanotechnologies promise to enable improvements in diagnostics and sensing, where a variety of nanotechnology platforms are being developed for applications within the food production chain (see Figure 7 below).

Figure 7. Schematic of the four main stages of the food value chain from farm to fork



Source: Adapted from Robinson, D. K. R. (2011), "Value chains as a linking-pin framework for exploring governance and innovation in nano-involved sectors: illustrated for nanotechnologies and the food packaging sector" European Journal of Law and Technology, 2(3).

This section presents examples of selected sensor technologies for food production, distribution and security. It provides an indication of the variety of developments in this area and is broken down into three application sub domains:

1. Agricultural production.
2. Food processing.
3. Packaging and distribution.

Scientific Research

In agricultural production, sensors and diagnostic devices enable farmers to closely monitor environmental conditions and plant and animal health and growth. As part of precision farming, they can facilitate targeted and early intervention, thus increasing productivity and decreasing use of agrochemicals (e.g. antibiotics, pesticides and nutrients). Sensors and diagnostic devices can be used to measure a number of important variables for agriculture, such as:

- The physiological status of crops (growth rates, nutritional levels, crop maturity, disease status);
- The physiological status of livestock (body temperature, respiration rate, blood biochemistry, disease status);
- The presence and identification of pests or pathogens; and
- Environmental variables (ambient temperature, levels of water and nutrients in soil).

They are also essential in measuring the environmental impact of the agricultural process itself, in particular the levels of pesticides and fertilisers in soil and run-off. A variety of different sensor and diagnostic systems based on nanotechnology have potential applications in the agricultural industry (see Figure 8).

Figure 8. Sensor systems that could be used in agricultural production

Technology	Description	Principle agents detected	Maturity
Single molecule sensors	Biomolecules enclosed by or attached to nanostructured materials such as liposomes, nanoparticles or carbon nanotubes. Detection is measured by electrochemical or optical readout.	Pesticides, gases.	Basic and applied research.
Bio-arrays	Biomolecules conjugated to substrates. Readout by chemical or electronic means.	Different chemical species and microbes.	Some mature, but application in the field still at the applied stage.
Solid-state sensors	Thin film or nanowire sensors. Readout by electronic means.	Gases.	Early-stage.
Optical and spectrographic sensors	Lasers and spectrometers.	Plant growth, presence of various chemical species.	Some mature, but application in the field still at the applied stage.
Sensor networks	Individual sensor nodes that can be dispersed throughout an area, measure local variables and report to a central processing unit.	Potentially all desired variables.	Microsystems technology is mature. Nanotechnology developments still at basic and applied research level.

Source: Adapted from Robinson, D. K. R. and M. Morrison, (2011), "Nanotechnologies for improving food quality, and security" In Editors: Frewer, L.,W. Norde, A. Fischer and F. Kampers, "Nanotechnology in the agri-food sector. Implications for the future" John Wiley and sons, Inc., New Jersey. Pages 107 – 126.

Biosensors utilise biomolecules to detect targets. However, the format of biosensors varies from free molecules to those bound to a substrate, such as nanoparticles, nanowires, nanotubes and thin-films. The interaction of the target with the biosensor can be measured either directly or indirectly via changes in, for example, colour, fluorescence and electrical potential. When placed in arrays, multiple biomolecules are fixed to a substrate allowing many things to be measured simultaneously.

For the agricultural and environmental industries, it is the development of technologies based on acetylcholinesterase (Vamvakaki and Chaniotakis, 2007) and tyrosinase (Sanz et al., 2005) which have drawn greatest interest. Acetylcholinesterase is an enzyme involved in nerve signalling in many different species and is inhibited by certain types of pesticides, as well as heavy metals. This inhibition can be measured by the failure of acetylcholinesterase to catalyse the conversion of substrate, or an analogue, that would normally result in its becoming more acidic. This increase in acidity can be measured electrochemically or by using a dye molecule that is sensitive to acid/alkali changes and exhibits a change in colour or fluorescence. Tyrosinase can catalyse the oxidation of phenolic compounds, which are present in many industrial wastewaters and are also used as pesticides.

Single molecule sensors can be either attached to an electrode or encapsulated in some form of matrix or other capsule. For nano-enabled technologies, liposomes (Viswanathan et al., 2006), self-assembled monolayers, carbon nanotubes (Chen et al., 2008) and nanoparticles show promise. Each provides increased sensitivity through the greater surface area of the nanoparticle which allows either more of the biomolecule to be present or greater access to the substance that is to be detected.

Whichever approach is used, the sensitivity is better than that required to detect the minimum legal safe limits. While acetylcholinesterase sensors are not specific to individual pesticides, they are cheap to

manufacture and useful for an overall measurement, and therefore could be a tool for rapid assessment in the field with follow-up in an analytical lab as required. However, to date there have been no field trials using such sensors with non-purified samples.

Array technologies, for example, can be used at different stages of the food chain such as: detecting the presence of pathogens in livestock or crops; measuring the levels of toxins or nutrients in soils; and monitoring the quality of processed food. Bio-arrays have the capability to simultaneously measure and quantify many different substances (in some cases thousands). Such arrays are a mature technology manufactured by a number of different companies and used in fields as diverse as clinical diagnostics, environmental monitoring and bioscience research.

Nanotechnology is beginning to have an impact on bio-arrays. The advantages that it brings to such systems are: further miniaturisation, allowing more variables to be measured; greater sensitivity, thus requiring less sample material; faster detection rates, allowing read-out in real time; and novel detection methodologies (e.g. electronic, colorimetric, fluorometric and mass changes).

Nanobio-arrays link several different biomolecules to a substrate in such a way that each is individually addressable. Arrays have been made using a number of different biomolecules, but have tended to concentrate on proteins (or parts of proteins) such as antibodies and enzymes, or DNA and RNA. These are quite mature technologies, having been developed and marketed by a number of companies for use in basic research and diagnostic sciences (including forensics and medicine). To date they have largely been based on microsystem technologies and used in laboratory settings for measuring analyte concentrations in semi-purified (e.g. filtered and buffered) samples.

Cantilever[33] arrays are perhaps one of the most interesting applications. They detect the presence of specific target molecules in a mixed environment through the binding of a reporter molecule that leads to mass displacement of the cantilever (McKendry et al., 2002). In addition, they can operate in gas or liquid phases, giving rise to the electronic "nose" and "tongue". One interesting example comes from the European Automated Water Analyser Computer Supported System (AWACCS) project which produced and field-tested an optical biochip capable of providing information on up to 32 different substances.

Product development and manufacturing

Precision agriculture

Global agriculture today faces many issues including maximising land-use in different environments, sustainable use of resources (in particular, fresh water) and ensuring that practices do not have an adverse impact on the environment (e.g. accumulation of pesticides and fertilisers). At the same time, there are opportunities for agriculture to expand into new areas and increase productivity in existing areas, for example, the use of what would previously have been regarded as agricultural waste in industrial processes. An area in which converged nanotechnology promises to contribute is that of "precision farming" (Robinson and Morrison, 2010).

This combination of nano- and info- (and often bio-) technology applies global positioning systems and networks of sensors and actuators throughout an agricultural area to measure and report on (and, in some cases, respond to) a number of different environmental, crop and pest variables. These effectively support the farmer by providing data that allows the farmer to make informed choices for irrigation, fertilisation, pest control and even harvest. Although costly, this is driven by the demand for higher quality produce and increasing legislative requirements.

Food processing

According to the European Food Safety Authority, there were a total of 5 311 foodborne outbreaks, involving 47 251 people and resulting in 5 330 hospitalisations and 24 deaths in 23 member states during 2005. The majority were caused by *Salmonella* and *Campylobacter* (EFSA, 2005). Many of these illnesses are caused by bacterial enterotoxins that are not easily removed from food as they are often stable at temperatures used in normal cooking. This can be combatted in part through the detection of food spoilage through bacterial, fungal or viral contamination at each stage in the food processing industry. This is a major market worth EUR 1.45 billion annually and with an estimated 558 million tests performed each year, 70% of which are for *Salmonella* and *Listeria*. More than 90% are performed by service laboratories but with an increasing use of rapid test kits.

In general, such systems must be able to detect the presence of 10-100 infectious particles per millilitre. There are various biosensor platforms in development that are based on nanostructured materials. While there is a large amount of research into the development of electronic approaches, there are also efforts in the area of optical and mass change detection (Pumera et al., 2007; Jaakohunta et al., 2007; McKendry et al., 2002). In each case, the nanostructured material includes biomolecules capable of interacting specifically with the target substance.

Most of these technologies are still at the level of basic research. However, Biophage Pharma Inc., in collaboration with the NRC-Biotechnology Research Institute, has developed electronic biosensors capable of distinguishing between different bacteria in a process termed Electric Cell-Substrate Impedance Sensing. This is now at the pre-commercialisation stage and is expected to have applications for the detection of bacteria in water, food and biological fluids.[34]

Food logistics and packaging

Food packaging acts to enclose food in a stable environment and protect it from environmental changes (such as moisture, light, oxidation and temperature), physical damage, and contamination by micro- (and macro-) organisms. Active packaging is an area in which nanotechnology is converging with informatics and is expected to have a large impact. Radio-Frequency IDentification (RFID) tags, temperature sensors and gas sensors based on nanomaterials are in development and in some cases have already been commercialised.

In conjunction with an effective packaging system, improvements in identification of items and stock control ensure that delivery is efficient and that foodstuffs are maintained in the appropriate conditions throughout the supply chain. This includes RFID tags for logging the movement of stock at all stages of the supply chain and other tags to provide covert or overt identification and authentication.

Smart packaging responds to its environment either by regulating an external effect or producing a visual readout of a change. It includes materials that can regulate the internal environment of packaged foodstuffs to maintain food quality (e.g. through the release or absorption of substances), sensors that provide an indication of the storage history of the product and whether it is still fresh, and materials which can repair minor damage (self-heal).

Regulating the internal environment of the packaging, at its simplest, is the control of the temperature of the foodstuff. Manufacturers of chilled or fresh foods want to ensure that their produce reaches the consumer in good condition. However, there are inevitable breaks in the cold chain, for example due to transfer between different transport systems. Sensor technologies for packaging should provide a visible indicator to the supplier or consumer that foodstuffs are still fresh, have been kept at the appropriate

temperatures throughout the supply chain, or has spoiled, or whether the packaging has been breached. Key factors in their use are cost, robustness, and compatibility with different packaging materials.

The ability to detect the presence of oxygen within packages, e.g. of fresh meat, at the earliest stage would alert the supplier or consumer that the packaging has been compromised, even if there are no visual indications of this. Such systems for the purpose of food packaging rely on changes in the colour of dyes in the presence or absence of oxygen. One commercialised microtechnology product is "Ageless Eye"[35] which is pink in the absence of oxygen and blue in its presence.

Advances using nanoparticles are expected to produce more sensitive systems that respond faster and produce stronger colour changes. For example, researchers at the University of Strathclyde have produced a hydroxyethyl cellulose polymer film oxygen sensor, containing titanium dioxide nanoparticles and the blue dye indigo-tetrasulphonate. Following incorporation into the packaging, the sensor is exposed to UV light and the dye is photobleached (a reaction catalysed by the titanium dioxide), remaining so until exposed to atmospheric oxygen levels. At this point it rapidly (within three minutes) returns to a deep blue colour, even in the dark (Mills et al., 2008).

Key observations[36]

This area of technology convergence exhibits much activity at the level of R&D, but little product-development dedicated to food safety and security. Although there is added value, the motivation to invest in novel technologies is low.

There is a disconnect between the industrial actors and researchers. A likely reason is that there have been relatively few opportunities for either vision building in this area or for making clear the requirements from the demand side (the food producers and processors).

Organised forums for visioning are very prominent in the nanomedicine examples provided earlier in this section. Vision building, sectoral demand articulation, and R&D roadmapping do not always occur naturally, however, and there is scope for policy actors to examine the utility of these activities.

III. POTENTIAL POLICY CONSIDERATIONS FOR NANO-RELATED CONVERGENCE

The entrance point of this report was to summarise what was meant by "converging technologies*"* and "technology convergence", then to explore technology convergence as it relates to nanotechnology via the use of Case Studies. Whilst it must be noted that this report has focused on only four of an ever-expanding number of applications, these suggest six potential areas for further policy consideration, discussed below.

Use of the term "converging technologies" is useful for priority setting but may lead to an innovation impasse

In discussions concerning converging technologies and technology convergence, there is an overlap in the use of the two terms. This not only causes confusion but also constitutes a bottleneck to innovation. Converging technologies and NBIC are umbrella-terms that are commonly used when discussing priorities and formulating policies. The term technology convergence, however, is best conceived as a description of actual instances of convergence at the level of research and innovation activities within laboratories and firms.

Thus the two terms correspond to separate sets of dynamics: one at the level of policy formulation and the other at the level of R&D activities. In early discussions about converging technologies, and NBIC in particular, these terms were useful in mobilising widespread engagement, interest and resources. At the time of writing this report, the terms converging technologies and NBIC are still used in discussions concerning priority setting and broader policy development, but there is very little reference to the term at the level of R&D activity and innovation.

Some recent studies have explored the relationship between the rhetoric associated with policy formulation and priority setting and the eventual reality in terms of resultant activities and deliverables, postulating in particular that overblown hyperbole can have a negative impact on actual outcomes. For example, a recent study (Robinson et al. 2012) explored "the innovation impasse", i.e. situations where raised expectations that have led to the stifling of R&D development and innovation. Similarly, concerning policies for "converging technologies", another study (Parandian *et al*., 2012) explored the role of hype and visioning in long-term priority setting and the consequences for "technology convergence" at the level of R&D and innovation-related activities.

Table 2 below (modified from Parandian *et al*., 2012), presents the key dynamics of situations that arise when the hype associated with the use of umbrella-terms like converging technologies begins to cause tensions with actual innovation processes. The 'waiting games' column indicates dynamics related to actual R&D and innovation activities; the other columns represent those related to converging technology.

The Table illustrates some of the key dynamics and outcomes that can lead to the stifling of developments in research and innovation, based on empirical examples that have been described in this report. Converging technologies are surrounded by big promises that envision a third industrial revolution, a sustainable world and human enhancement, and these strongly influence priority-setting. At the same time, however, the diffuse and open-ended nature of these promises can be an obstacle to the realisation of envisaged benefits. They make actors uncertain about directions to take and thus create a reluctance to invest in concrete developments (the 'waiting games' column in Table 2). A gap can be observed between promises couched in terms of achieving broad social goals and specific R&D technological attainments.

Such promises and projections often do not take into account the realities of product development and the limited coupling with scientific research, as demonstrated in earlier sections of this report.

Table 2. Promise dynamics and their outcomes related to convergence

	Hype and hope[1]	Promise icons	Priority setting	Waiting games
Dynamics	While technology developers are concerned about possible disappointment, exaggeration is perceived to be inevitable to create visibility and attract funding. Umbrella promises are hype-friendly.	Concrete technology developments refer back to umbrella promises which remain unchecked. Success in developments is attributed to the "force" of the umbrella promise, while failure is related to other factors.	Umbrella promises invite priority setting and funding (related to grand challenges). Long-term goals are more important than concrete innovation.	Appealing umbrella promises keep actors "in the game", while uncertainties about demand from users and uncertainties about specific technology directions make the interdependent actors reluctant to take concrete action.
Outcomes	Big umbrella promise eventually collapses, a shake-out occurs, work continues on the few technologies that show concrete promise.[2]	Umbrella promises survive, despite failures in concrete technology developments which refer back to them.	With their partial institutionalisation, umbrella promises provide stable backdrop for agenda-building and acquisition of funding.	Actors recognise umbrella promises, but will not take the risk of investing heavily in concrete developments until the situation is clearer.
Empirical examples	"Converging Technology" as a hype at the beginning of 2000s fits this dynamic. Promises strongly tied to those of nanotechnology created visibility and attracted funding.	Kevin Warwick's promise of human implants (Warwick 2004), referring to the Human Enhancement element of NBIC, but little elsewhere. R&D focuses on fundamental nerve-computer interfacing.	NBIC originally as a visioning exercise triggered debate and interest providing a backdrop for discussions of convergence and of nanotechnology. Today NBIC2[3] plays a similar role.	Visible in the case of lab-on-a-chip technologies.

Source: Robinson, D. K. R., A. Porter and Y. Guo, (2012), "Vector platforms for nano-enhanced drug delivery: capturing innovation pathways in the making" Paper presentation at the International Conference on Innovative Methods for Innovation Management and Policy, Beijing, May 2012 (adapted with permission from Parandian, A., A. Rip and H. te Kulve, (2012), "Dual dynamics of promises, and waiting games around emerging nanotechnologies" Technology Analysis & Strategic Management, 24(6), 565-582.)

Notes : [1]Hype can be defined as large open-ended promises that drive interest and excitement in a field of technology. The promises may be well grounded or unfounded, regardless of which they have influence and drive investment of resources and increase interest in a field. Hype is common in priority setting and is regarded as common practice in technology R&D and innovation (van Lente et al. 2013).

[2]. Following the Gartner Group Hype Cycle. A good introduction to the hype-cycle model can be found at: http://en.wikipedia.org/wiki/Hype_cycle

[3]. For example see the NBIC2 workshop held in December 2012 in Arlington, United States. www.wtec.org/NBIC2/

The mismatch between "converging technology" discussions and the concrete activities of innovation actors is an important point that requires further investigation. If this disconnect continues, there is a clear danger that innovation based on instances of convergence in the research domain will be limited.

Firms may be interested in exploiting the knowledge produced by convergent research but lack clarity concerning aspects of the necessary technology production infrastructure (manufacturing processes, standards, regulations, etc.). There is little incentive for them to make the first move into the unknown, leading to individual firms adopting waiting strategies. When this occurs collectively, innovation deadlock can result.[37] For example, the complex and uncertain interactions and dependencies between multiple actors in nanomedicine provides a challenging environment for innovation and societal uptake.

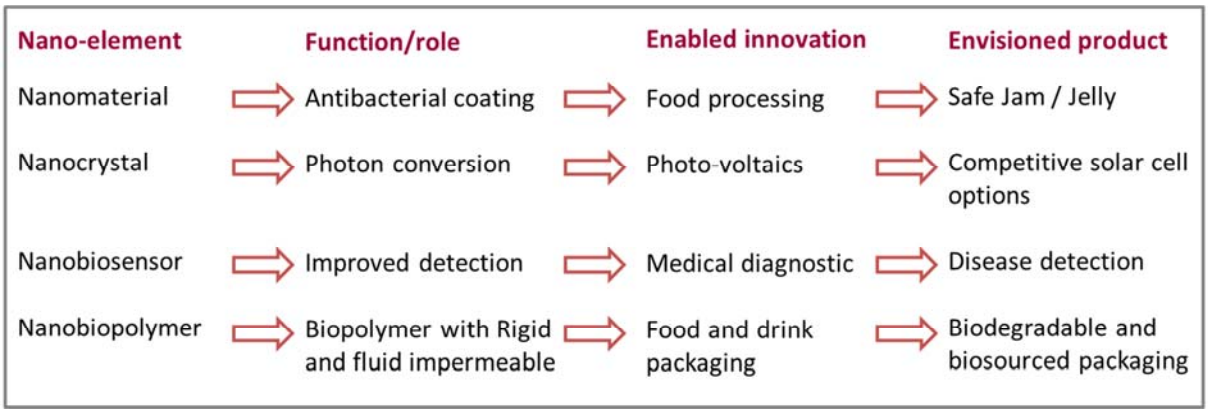
Uncertainties in terms of risk, acceptance by patients (public) and the scope of future developments in nanomedicine means that companies and manufacturers of medical products are often very cautious, preferring to wait and watch rather than acting rashly.

The impact of nanotechnology depends on its utilisation in the value chain

Nanotechnology research involves the manipulation of nanoscale structures and the exploration of their properties. This can result in a diverse array of nanomaterials and nano-objects that promise to play a role in many sectors (both products and manufacturing processes).

Figure 9 below provides examples of value chains from selected nano-elements to possible end-products. Nanotechnologies can enable products in a variety of ways: the nanotechnology itself could be central to the functioning of a product (e.g. a nanobiopolymer may be the key enabling technology for a product), or it could add value along with a number of other elements of a technology (e.g. a nanocrystal or nanobiosensor may only be useful when combined with other technologies). Nanotechnology can also enable process technologies that improve a product (e.g. improved safety from using nano-antibacterials in a process) but where the nanotechnology itself is not part of the final product.

Figure 9. Four examples of value chains where nanotechnology adds value in a variety of ways



Source: Adapted from Robinson, D. K. R. and A. Rip, (2012), "Socio-economic Dynamics of Innovation and Uptake" Joint OECD/NNI International Symposium on Assessing the Economic Impact of Nanotechnology, Washington. March 27- 28.

Of importance here is that the impact of nano-involved technology convergence will depend on its role in the innovation chain. This is also important for the evaluation of socio-economic impacts of nano-involved technology convergence, which is the subject of the next sub-section.

Industrial domain and application contexts influence impact pathways

From the examples given in Section II, it can be demonstrated that impacts of nano-involved technology convergence are distributed across value chains. It can also be argued that socio-economic impacts are not nano-specific but rather domain-specific and application-specific.

Therefore, impact assessments should recognise that innovation and uptake (and therefore the impacts of nano-related converging technologies) are distributed, that the key value added may occur at quite a distance from the laboratory where the techno-scientific knowledge originated, and that final success and final impact are realised when nano-related developments are embedded in actual products and processes.

Although impact chains can be long and complex, studies of innovation and societal uptake processes for nanotechnologies have revealed that there are patterns in the way nanotechnologies are impacting markets and society. Although these studies focus on nanotechnology, there may be lessons for nano-related technology convergence. One study by Robinson and Rip (2012) suggests that there are specific impact pathways that nanotechnologies may follow in the way they impact markets and society. Box 1 provides an edited example of the four pathways identified for nanosensors.

Box 1 Four impact pathways for nanosensors[1.]

Impact Pathway 1: A path clearly marked out

This pathway occurs when there is a combination of high performance technology with small dedicated markets. For example, in aeronautic and space applications, the large organised design and deployment process means that the intended impacts of a nanosensor technology in the aerospace domain are clearly defined and can be followed and evaluated. One can use the original goals linked to technology readiness levels as impact descriptors.[2.]

Impact pathway 1 is common in large scale innovation organisations. Continuing with the domain of aerospace, organisations such as NASA, ESA, Lockheed Martin and Astrium have large systems engineering processes which integrate the various technologies into working configurations, such as space systems and aircraft. There is a highly structured and closely-connected value chain.

Impact Pathway 2: A road that leads to another

This pathway occurs in highly structured, closely-connected value chains in which the demonstration of the technology in one domain leads to exploration of its application in another domain. One example would be diagnostic technologies in hospitals. Medical nanosensors (which require a near zero-failure rate) for the detection of elements in blood, lymph and urine, demonstrate value and application in agriculture where sensors and diagnostic devices allow farmers to closely monitor environmental conditions, and plant and animal health and growth. As part of precision farming or high-tech nurseries they can facilitate targeted and early intervention, increasing productivity and decreasing the use of agrochemicals.

However, uptake of nanosensors in the field of precision farming is heavily dependent on its demonstration elsewhere, its cost and its reliability. Thus, indications of impact for impact pathway 2 would be linked to the pollination from one domain (which has demonstrated the value of a new technology) into another. This pathway is distinct in its effects from impact pathway 1, but may of course follow on from impact pathway 1. Therefore, tracing impacts related to pathway 2 would require monitoring of the possible branching from one domain to another (cf. medical to agriculture).

Impact Pathway 3: A looping path related to evolving user -context

This pathway involves an evolution of the technology and its use-context. Initially there will be market projections by technology developers for the new technology on the basis of existing user roles and their responsibilities. After introduction and uptake of the novel technology, there is an intermediary social impact involving changes in roles and responsibilities of both users and technology developers (including new actors emerging in and around the value chain). Larger/different markets may emerge (the loop), and so other impacts. Evaluating the socio-economic impacts with innovation processes following this pathway would have to take this non-linearity into account. An example is point-of-care devices for self-diagnostics and possible self-medication.

Performance for these technologies must be relatively high, based on reliability, but the market can become large when the roles of doctors, healthcare professionals and patients shift (and insurers agree). Interesting in the case of point - of - care diagnostics is the attempt to control self-diagnosis in the Netherlands, but which resulted in patients buying such products on the Internet from a company based in the Czech Republic. Indications of impact are linked to the first order loop of development (performance of technology and penetration into user area) and also indications of impact in terms of new roles and new markets (the creation of them, the rate and spread of change).

Impact Pathway 4: Low performance and multiple applications

This pathway relates to the business model of low performance and large markets. Here, application of knowledge from a new field of technology is attempted early with relatively simple technological applications. High performance is not a requirement, but added value of the new technology is seen. Low performance nanosensors could be applicable to many value chains, providing added value to existing technologies in a small way.

An example for nanosensors is in clothing, where patches worn on the body become part of the clothes. Sensors for salt (in sweat), heart rate, temperature and other characteristics are in development. Here, there is less of a need for high accuracy (with respect to medical needs). Their use spreads to clothing for outdoor sports activities or fitness centres. Sensors in clothing also play a role in comfort. Demand for these product applications stem less from societal need, but from cultural trends such as wealth demonstration and the new importance of lifestyle and the economy of experience. Impacts of low performance nanosensors will be broad and diffuse, as a result of many intersecting value chains.

Notes: [1.] Adapted text from the forthcoming chapter Robinson and Rip (2013).
[2.] An example is the use of advanced magnetic nanosensor technology for exploration of Mars or Mercury (Nanowerk 2013). For more details on the technology, see Sensitec GmbH : http://sensitec.com.p-ad.de/english/technology/mr-sensor-technology/mr_sensortechnologie.html

The role of nano-involved technology convergence can vary in the development of particular technology products and creates a challenge for assessment and evaluation. As described in the Box, the domain contexts and the types of innovation and uptake processes will have an effect on the types of socio-economic impacts that have to be measured. With this in mind, further investigation into the impact pathways of nano-involved technology convergence could have merit.

Public engagement in the design and deployment of converging technologies should be explored

Public engagement around nano-enabled converging technologies is expected to become increasingly important in the next five years. This is linked to the maturation of nanotechnologies themselves and their deployment in devices, drug delivery, and potentially in food security etc. Insights for effective action are included in the OECD "Planning Guide for Public Engagement and Outreach in Nanotechnology" (OECD, 2012), and work and thinking in this area continues.

Public engagement can take two forms. One is engagement in communication, to make transparent the activities in converging technologies and inform citizens. To date, there have been many public engagement activities in and around nanotechnologies for the purpose of awareness building and education (see Rogers-Hayden et al., 2007)

A second way that the public can be engaged is in the development and use of specific technologies. In medical technologies, this can call for the involvement of patient groups, and elsewhere other actors can be involved in the deployment of new technologies.[38] For example, the activities and involvement of social scientists can be important, especially those engaged in Science and Technology Studies (STS)[39] focusing on issues related to nanotechnology, converging technologies and various processes of engagement and involvement in the design and development of technologies.

Regulation of converging nanotechnologies needs to be considered

Converging technologies bring with them challenges for regulation. This is particularly noted in areas of convergence in the healthcare sector, especially in the area of nanomedicine, which is already entering/stimulating value chains and in some cases entering markets. The case of nanomedicine highlights

some of the challenges, although it must be acknowledged that different areas of convergence will have different regulatory structures and legislative cultures.

Regulatory and legislative strategies and structures continually need to evolve to cope with technological change. Convergence promises evolution along multiple routes, and at a rapid pace, and thus it may be necessary to create regulatory and legal instruments able to respond rapidly and on multiple fronts. It is likely to prove useful to explore governance approaches and their timing in representative examples of converging technologies in which nanotechnologies play a role.

A final point highlighted in recent work by Desmoulin-Canselier (2012) is worth noting. This noted that measures to prohibit human cloning refer more to the actual use of cloning techniques than they do to the knowledge-embedded in the techniques. Thus the prohibition on human cloning does not affect freedom of research nor does it restrict dissemination of the resultant knowledge. This raises an issue for the regulation of technologies based on convergence that may be used for unethical (or prohibited) applications. Policy-makers need to consider what should be regulated - regulating the "use" versus regulating the "knowledge". It is predicted that this difference between regulating "use" and "knowledge" may become an increasingly discussed issue.

The role of responsible research and innovation

Some of the potential environmental and health risks that have been associated with nanomaterials have given rise in some quarters to calls for "anticipatory governance" (Barben et al., 2007) or "responsible development and innovation" (von Schomberg, 2007). In essence, these attempt to constrain the development and diffusion of harmful technologies and encourage the genesis and spread of beneficial ones by specifically taking societal needs into account when framing policies.

Current debates about responsible development and innovation distinguish between interventions that focus primarily on controlling the use of technologies via regulatory policies and those that attempt to stimulate or constrain scientific and technological developments that are respectively deemed "wanted" or "unwanted". Attempts to restrict developments at the level of R&D activities have been particularly noticeable, including calls for moratoria on nanoparticle R&D and synthetic biology research, and the Code of Conduct for Nanoscience Research, proposed by the European Commission in 2008[40], made specific reference to "responsible research".

The interest in responsible research and innovation is unlikely to wane. In February 2013, the European Commission published "Options for Strengthening Responsible Research and Innovation" [41] and launched four large projects on the topic[42]. Concerning nano-related technology convergence, the adoption of "anticipatory governance" regimes will be complicated by the myriad impact pathways nano-related developments are expected to follow, but efforts will still need to be made to evolve responsible development strategies if public controversy is not to be courted.

CONCLUSION

In terms of **technology convergence**, new communities are emerging around new combinations of technologies, some of which have potentially important implications for innovation in a broad range of application domains. Four examples of nano-enabled convergence are examined in this report.

Section III summarised some of the lessons for policy development that are suggested by these case studies, ranging from the need to temper ambitious expectations with a healthy dose of realism to suggestions concerning attempts to assess impacts and the need for a strong policy focus on public engagement, regulation and "responsible development".

However, policy-makers should apply caution when considering these policy suggestions. The design of policies catering for emerging and converging technologies is complicated by the rapid pace of innovation and change and long-term trends cannot easily be identified. In addition, it is always dangerous to generalise from a limited number of case studies.

It must also be recognised that country and regional variations will play a key role in determining the most applicable lessons to be drawn from this report. The way in which technology convergence both occurs and leads to new products and processes in different application areas is highly context specific. Although some of the general points made in this report, e.g. concerning the need for greater public engagement and sustainable development, are likely to hold, the policy responses to them will depend greatly on the social, political and economic milieus in which they are addressed.

That said, when contemplating customised policy options, the material contained in this report suggests that policy interventions concerning nanotechnology-related technology convergence might best be focused:

- On specific instances of convergence (e.g. on specific research fields like nanobiotechnology or synthetic biology);
- Along particular value chains (e.g. neurotechnology and targeted drug delivery);
- On attempts to embed technologies into particular application areas corresponding to societal needs (e.g. nanofoods and green packaging).

NOTES

1 The technological augmentation of human capabilities and modification of the human body and intellect.

2 Although converging technologies have been argued to have occurred before, in the 2000s the concept placed at its core the combination, fusion and synergies between different fields of research.

3 "*White Paper on Nanotechnology Risk Governance":* www.irgc.org

4 http://ec.europa.eu/bepa/european-group-ethics/index_en.htm

5 http://wtec.org/NBIC2/

6 For clarification purposes it is important to make some distinctions on forms of cross-disciplinary R&D. *Multi-disciplinary* R&D draws on knowledge from different disciplines but stays within the boundaries of one particular discipline whereas *Inter-disciplinary* R&D links disciplines together into a co-ordinated and coherent whole (a new field glued together with shared goals and R&D processes).

7 For a more complete discussion, see the paper of the Working Party on Biotechnology on "Policies for Bioplastics in the context of a Bioeconomy"; http://dx.doi.org/10.1787/5k3xpf9rrw6d-en

8 European Regulation No. 1935/2004 requires approval to be granted before a substance is authorised for use in food contact materials.

9 World patent number 0240579: Coated films and coating compositions.

10 www.igdhs.ch/

11 www.etcgroup.org/issues/nanotechnology

12 www.soilassociation.org/

13 It is not part of this report to go deep into the regulatory landscape of each innovation area. However, important to note is that here are many regulatory landscapes influencing the development of converging technologies. For example, in nano-enabled food packaging, non-nano-specific regulation includes the regulation of food contact plastics which are subject to additional measures regulated by Regulation (EC) 282/2008 on recycled plastic materials and articles, and by Regulation (EC) No 450/2009 which sets down additional requirements to Regulation (EC) No 1935/2004 for active and intelligent materials and articles. The Plastic Implementation Measure (PIM) - 14262/10, the regulation on plastic materials and articles intended to come into contact with food, came into force May 2011. It affects the use of nano-based food packaging in the EU as it states clearly that plastics that use nanomaterials should be assessed on a case-by-case basis until more information is known about the potential risks they present.

14 The European Food Safety Authority (EFSA) is an independent source of scientific advice and communication (supporting the European Commission, the European Parliament and EU Member States) in taking effective and timely risk management decisions on risks associated with the food chain. EFSA's remit covers food and feed safety, nutrition, animal health and welfare, plant protection and plant health.

15 www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178678338323.htm.

16 See http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:338:0004:0017:EN:PDF.

17 The FSA regulatory review "A review of potential implications of nanotechnologies for regulations and risk assessment in relation to food" (August 2008) has not identified any major gaps in regulations relating to the use of nanotechnologies in food.

18 It should be noted that the 27 Member States of the European Union along with four additional States were selected because the European Commission provides significant research support to the 31 countries.

19 www.clinam.org.

20 In addition to the potential risks associated with nanomedical products themselves, a number of commentators have raised concerns about the potential occupational and environmental risks associated with the manufacture and disposal of nanomedicines, drugs and devices (Marchant et al. 2009). Regulators are increasingly faced with the need to regulate nanomedicine, while knowledge gaps, questions of expertise and definitional issues all pose crucial challenges

(Chowdhury, 2010). As in many other areas, there are no specific laws pertaining to nanomedicine in the European Union (EU), nor indeed in any other jurisdiction, at this time. However, this does not mean that nanomedicine is "unregulated". Rather, such products are being regulated under existing legislation on medicinal products and devices, tissue engineering and other advanced therapies. See also www.oecd.org/science/nanosafety/

21 http://ec.europa.eu/enterprise/policies/european-standards/harmonised-standards/medical-devices/

22 It is also important to note that the regulatory regime for medical devices is different from that of drugs. Thus, the costly development and regulatory approval of pharmaceuticals compared with the relatively low cost of medical devices means there is an economic incentive to switch to neurotechnologies.

23 www.kevinwarwick.com/

24 Leading to much debate on the nature of what it is to be healthy and to be human, often the focal point of discussions on ethical aspects of converging technologies.

25 The majority targeted at Parkinson's.

26 FRONTIERS was a European Framework Programme Network of Excellence that ran between January 2004 – June 2008.

27 IMEC is a laboratory for advanced research in micro and nanoelectronics based in Leuven, Belgium. www.imec.be

28 Further details of this project are available in Robinson et al. (2013).

29 In fact, they continue to this day (see Ferrari et al. 2012).

30 This article in Nature Nanotechnology is quoted as Nordmann and Rip to provide a clear concise message about speculative ethics, which resonates with the debate about converging technologies.

31 For detailed examples of these tools and approaches applied to areas of converging technologies (from the nanotechnology perspective) see Parandian (2012) for Body-Area-Networks and Robinson (2010) for Deep-Brain-Stimulation and Cell-on-a-Chip technologies.

32 Many of these were presented at a recent workshop organised by the OECD and the United States National Nanotechnology Initiative (see www.nano.gov/node/729).

33 Cantilevers are small structures resembling diving boards at a swimming pool. Generally a detection element is attached at the end of the diving board and when a reaction with the intended substance takes place the board, or "lever", bends. It is this bending that is measured and turned into a measurable signal.

34 Biophage Pharma Inc. website, accessed 21.10.08: www.biophagepharma.net/index.php?option=com_content&task=view&id=30&Itemid=40

35 Mistubishi Gas Chemical Co. www.mgc.co.jp/eng/products/abc/ageless/eye.html

36 In this example, there is little data on societal and governance aspects of converging technologies for food safety and quality control. This is a consequence of the limited product development activities which would act as a trigger for societal debate and governance activities. With this in mind, the section on societal aspects and governance has been omitted.

37 This topic is explored in detail in a special issue of the Journal of Technology Analysis and Strategic Management, July 2012 issue, see Robinson, D. K. R., A. Porter and Y. Guo, 2012.

38 Another example of when the public might be included in the design process is related to labelling. The development of the appropriate labelling approaches to inform consumers should involve interaction with the consumers themselves. This is less clear in the case outlined in section I-4 on the labeling debate.

39 One such community dedicated to the study of nanotechnologies and related emerging technologies is the Society for Nanotechnology and Emerging Technologies (S-NET) which creates an annual forum and produces publications on the latest activities in analyses of emerging technologies and multi-stakeholder involvement.

40 Commission Recommendation on a code of conduct for responsible nanosciences and nanotechnologies research. C(2008) 424 final (07/02/2008).

41 Published on the 15th February 2013: www.ukrio.org/european-commission-report-on-responsible-research-and-innovation/

42 The GREAT project, Res-Agora, Progress and Responsibility. For more details, see the joint meeting of all four projects at the following link : www.great-project.eu/presentation/kickoff.

REFERENCES

Barben, D., E. Fisher, C. Selin, and D. H. Guston (2007), "Anticipatory Governance of Nanotechnology: Foresight, Engagement, and Integration" The handbook of science and technology studies, 979.

Boyd, B. J. (2008), "Past and future evolution in colloidal drug delivery systems" Expert Opinion Drug Delivery 5(1): 69-85.

Burri, R.V. and S. Bellucci (2008), "Public perception of nanotechnology" J. Nanopart. Res. 10, 387 – 391.

Carothers, J. M., J. A Goler and J. D. Keasling (2009), "Chemical synthesis using synthetic biology" Current opinion in biotechnology, 20(4), 498.

Chen, H. D., X.L. Zuo, S. Su, Z.Z. Tang, A. B. Wu, S. P. Song, D. B. Zhang, and C. H. Fan, (2008), "An electrochemical sensor for pesticide assays based on carbon nanotube-enhanced acetycholinesterase activity" Analyst, 133, 1182-1186.

Chowdhury, N. (2010) "Regulation of Nanomedicines in the EU: distilling lessons from the paediatric and the advanced therapy medicinal products approaches" Nanomedicine 5(1):135-142.

Cobb, M.D. and J. Macoubrie, (2004), "Public perceptions about nanotechnology: risks, benefits and trust" J. Nanopart. Res. 6, 395 – 405 .

D'Silva, J. and D. Bowman, (2011) "The Regulation of Nanomedicine", in Hunter, R and V. Preedy, (eds), "Nanomedicine in Health and Disease" Science Publishers, USA: 20-42.

D'Silva, J. and G. Van Calster (2010) "For me to know and you to find out? Participatory mechanisms, the Aarhus Convention and new technologies" Studies in Ethics, Law and Technology, 4(2): 1-34.

Dalmas F., J. Y. Cavaillé, C. Gauthier, L. Chazeau and R. Dendievel, (2007), "Viscoelastic behaviour and electrical properties of flexible nanofibre filled polymer nanocomposites. Influence of processing conditions" Composites Science and Technology, 67, 829–839.

de Azeredo H.M.C. (2009), "Nanocomposites for food packaging applications" Food Research International 42 (2009) 1240–1253.

DEFRA (2011) Government Review of Waste Policy in England 2011: www.defra.gov.uk/publications/files/pb13540-waste-policy-review110614.pdf.

Desmoulin-Canselier, S. (2012) "What Exactly Is It All About? Puzzled Comments from a French Legal Scholar on the NBIC Convergence" NanoEthics, 1-13.

EFSA (2005), "The Community Summary Report on Trends and Sources of Zoonoses, Zoonotic Agents, Antimicrobial resistance and Foodborne outbreaks in the European Union in 2005": (www.efsa.eu.int/EFSA/efsa_locale-1178620753812_1178620767319.htm)

EFSA (2008), "Call for Scientific Data on Applications of Nanotechnology and Nanomaterials used in Food and Feed":

(www.efsa.europa.eu/en/dataclosed/call/sc080123.htm)

EFSA (2009) Scientific Committee's "Scientific opinion on "The Potential Risks Arising from Nanoscience and Nanotechnologies on Food and Feed Safety", adopted 10 February, EFSA Journal, 958, 1–39.

ETAG (2006), "Technology Assessment on Converging Technologies" Report commissioned by the European Parliament implementing Framework Contract IP/A/STOA/FWC/2005-28.

Ferrari, A., C. Coenen and A. Grunwald, (2012), "Visions and Ethics in Current Discourse on Human Enhancement" NanoEthics, 1-15.

Food Standards Agency, (2011), "FSA Citizens Forums: Nanotechnology and food" TNS-BMRB Report JN 219186, April 2011.

Fromherz, P, A. Offenhauser, T. Vetter and J. Weis, (1991), "A neuron-silicon junction- A Retzius cell of the leech on an insulated- gate field-effect transistor" Science 252, no. 5010 (1991): 1290-1293.

Gaskell, G., T. Ten Eyck, J. Jackson and G. Veltri, (2005), "Imaging nanotechnology: cultural support for technological innovation in Europe and the United States" Public Underst. Sci., 14, 81 – 90.

Greiner, R. (2009), "Current and projected applications of nanotechnology in the food sector" Nutrire: rev. Soc. Bras. Alim. Nutr. J. Brazilian Soc. Food Nutr., São Paulo, SP, v. 34, n. 1, p. 243-260.

Grunwald, A. (2007), "Converging technologies: Visions, increased contingencies of the conditio humana, and search for orientation" Futures, 39(4), 380-392.

IG DHS (2008), Factsheet Code of Conduct for nanotechnologies. Retrieved 23-10-2008: www.igdhs.ch/m/mandanten/190/topic6220/story14345.html

Jaakohunta, S., H. Harma, M. Tuomola and T. Lovgren, (2007), "Sensitive Listeria spp. immunoassay based on europium(III) nanoparticulate labels using time-resolved fluorescence" International Journal of Food Microbiology, 114, 288-294.

Khushf, G. (2006), "Systems theory and the ethics of human enhancement: a framework for NBIC convergence" Annals of the New York Academy of Sciences, 1013(1), 124-149.

Kim, S., I.K. Kwon, I.C. Kwon and K. Park, (2009), "Nanotechnology in Drug Delivery: Past, Present, and Future" In Nanotechnology in Drug Delivery eds. De Villiers, M.M., Aramwit, P. and Kwon, G.S. Springer: 581-596.

Lagaron, J. M., L. Cabedo, D. Cava, J. L. Feijoo, R. Gavara and E. Gimenez, (2005), "Improving packaged food quality and safety" Part 2: nanocomposites. Food Additives and Contaminants, 22(10).

Limousin, P., P. Krack, P. Pollak, A. Benazzouz, C. Ardouin, D. Hoffmann and A. L. Benabid, (1998), 'Electrical stimulation of the subthalamic nucleus in advanced Parkinson's disease' New England Journal of Medicine, 339(16), 1105-1111.

Marchant, G. E., D. J. Sylvester and K.W. Abbott (2009), "What does the history of technology regulation teach us about nano oversight?" Journal of Law, Medicine and Ethics, 37: 724-731.

Marsh, K. and B. Bugusu, (2007), "Food Packaging—Roles, Materials, and Environmental Issues" Journal of Food Science, 72, R39-R55.

McKendry, R., J. Y. Zhang, Y. Arntz, T. Strunz, M. Hegner, H. P. Lang, M. K. Baller, U. Certa, E. Meyer, H.J. Guntherodt and C. Gerber, (2002), "Multiple label-free biodetection and quantitative DNA-binding assays on a nanomechanical cantilever array" Proceedings of the National Academy of Sciences of the United States of America, 99, 9783-9788.

Miller, G. (2010), "Is pharma running out of brainy ideas?" Science, 30 July. Vol. 329, p.502-504.

Milleson, V. (2013), "Nanotechnology, the Brain, and the Future: Ethical Considerations" In Nanotechnology, the Brain, and the Future, pp. 79-96. Springer Netherlands, 2013.

Mills, A., C. Tommons, R.T. Bailey, M. C. Tedford and P.J. Crilly, (2008), "UV-activated luminescence/colourimetric O-2 indicator" International Journal of Photoenergy, 6.

Nordmann, A. (2004), "Converging Technologies – Shaping the Future of European Societies" HLEG Foresighting the New Technological Wave.

Nordmann, A. and A. Rip, (2009), "Mind the gap revisited" Nature nanotechnology, 4(5), 273.

OECD 2012, *Planning Guide for Public Engagement and Outreach in Nanotechnology*

OECD 2013, *Regulatory Frameworks for nanotechnology in foods and Medical Products: Summary Results of a Survey Activity*

Parandian, A., A. Rip and H. te Kulve, (2012), "Dual dynamics of promises, and waiting games around emerging nanotechnologies" Technology Analysis & Strategic Management, 24(6), 565-582.

Pumera, M., S. Sanchez, I. Ichinose and J. Tang, (2007), "Electrochemical nanobiosensors" Sensors and Actuators B-Chemical, 123, 1195-1205.

Ramakrishna, S., K. Fujihara, W.E. Teo, T. Yong, Z. Ma and R. Ramakrishna, (2006), "Electrospun nanofibers: Solving global issues" Materials Today, 9, 40–50.

Rip, A., T. J. Misa and J. Schot, (1995), "Managing technology in society" Pinter Publishers.

Robertson, G. L. (2006), "Food Packaging: Principles and Practice" Second Edition.

Robinson, D. K. R. and G. Salejova, (2010), "Nanotechnology for Biodegradable and Edible Food Packaging" Focus Report for the ObservatoryNANO project, 7th Framework Programme.

Robinson, D. K. R., L. Huang, Y. Guo and A. L. Porter (2013), "Forecasting Innovation Pathways (FIP) for new and emerging science and technologies" Technology Forecasting and Social Change doi:10.1016/j.techfore.2011.06.004.

Robinson, D. K. R., A. Porter and Y. Guo, (2012), "Vector platforms for nano-enhanced drug delivery: capturing innovation pathways in the making" Paper presentation at the International Conference on Innovative Methods for Innovation Management and Policy, Beijing, May 2012.

Robinson, D. K. R. and T. Propp, (2008), "Multi-path mapping for alignment strategies in emerging science and technologies" Technological Forecasting and Social Change, 75(4), 517-538.

Robinson, D. K. R. and T. Propp, (2011), "Innovation-chain+ approach to prospecting technology embedding in society" Fourth International Seville Conference on Future-Oriented Technology Analysis (FTA), FTA and Grand Societal Challenges – Shaping and Driving Structural and Systemic Transformations, Seville, 12-13 May 2011. foresight.jrc.ec.europa.eu/fta_2011/documents/.../ROBINSON.doc

Robinson, D.K.R. (2010), "Constructive Technology Assessment of Emerging Nanotechnologies: Experiments in Interactions" PhD Manuscript, University of Twente, The Netherlands.

Robinson, D. K. R. (2011), "Value chains as a linking-pin framework for exploring governance and innovation in nano-involved sectors: illustrated for nanotechnologies and the food packaging sector" European Journal of Law and Technology, 2(3).

Robinson, D. K. R. and M. Morrison (2010), "Nanotechnology for the Agrifood sector – emerging innovations", Conference paper presented at the 28th International Horticultural Congress, Lisboa, 23 August.

Robinson, D. K. R. and M. Morrison, (2011), "Nanotechnologies for improving food quality, and security" In Editors: Frewer, L.,W. Norde, A. Fischer and F. Kampers, "Nanotechnology in the agri-food sector. Implications for the future" John Wiley and sons, Inc., New Jersey. Pages 107 – 126.

Robinson, D. K. R., Rip, A. and V. Mangematin, (2007), "Technological agglomeration and the emergence of clusters and networks in nanotechnology" Research policy, 36(6), 871-879.

Robinson, D. K. R. and A. Rip, (2012), "Socio-economic Dynamics of Innovation and Uptake" Joint OECD/NNI International Symposium on Assessing the Economic Impact of Nanotechnology, Washington. March 27- 28.

Robinson, D. K. R. and A. Rip (2013), "Indications of socio-economic impacts of nanotechnologies" Chapter forthcoming in the edited volume of the fourth annual conference of the Society for the study of Nanoscience and Emerging Technologies (S-NET). www.utwente.nl/igs/conference/2012_snet_conference/

Roco, M. and W. Bainbridge, (eds) (2002), "Converging technologies for improving human performance" Nanotechnology, biotechnology, information technology and cognitive science. National Science Foundation, United States

Rogers-Hayden, T., A. Mohr and N. Pidgeon, (2007),"Introduction: engaging with nanotechnologies–engaging differently?" NanoEthics, 1(2), 123-130.

Sanz, V. C., M. L. Mena, A. Gonzalez-Cortes, P. Yanez-Sedeno and J.M. Pingarron, (2005), "Development of a tyrosinase biosensor based on gold nanoparticles-modified glassy carbon electrodes - Application to the measurement of a bioelectrochemical polyphenols index in wines" Analytica Chimica Acta, 528, 1-8.

Schuurbiers, D., S. Sleenhoff and D. Bennett, (2007), "Issues to be raised: ethical and social considerations in nanotechnology research" Philosophy & Engineering, 72.

Siegrist , M., N. Stampfli, H. Kastenholz and C. Keller, (2008), “Perceived risks and perceived benefits of different nanotechnology foods and nanotechnology food packaging” Appetite , 51 , 283 – 290.

Swierstra, T., R. Van Est and M. Boenink, (2009), “Taking Care of the Symbolic Order. How Converging Technologies Challenge our Concepts” NanoEthics, 3(3), 269-280.

Torres-Giner, S., M.J. Ocio and J.M. Lagaron, (2008),”Development of Active Antimicrobial Fiber-Based Chitosan Polysaccharide Nanostructures using Electrospinning” Engineering in Life Sciences Volume 8 Issue 3, Pages 303 – 314.

Vamvakaki, V. and N. A. Chaniotakis, (2007), “Pesticide detection with a liposome-based nano-biosensor” Biosensors & Bioelectronics, 22, 2848-2853.

van Est, R. and D. Stemerding, (2012), “Making Perfect Life - European Governance Challenges in 21st Century Bio-engineering” Final Report.

van Lente, H, C. Spitters and A. Peine, (2013),”Comparing technological hype cycles: Towards a theory” Technological Forecasting and Social Change (2013).

von Schomberg, R. (2007), “From the ethics of technology towards an ethics of knowledge policy & knowledge assessment” A working document from the European Commission Services. Brussels: European Commission.

Viswanathan, S., L. C. Wu, M.R. Huang and J. A. A. Ho, (2006) “Electrochemical immunosensor for cholera toxin using liposomes and poly(3,4-ethylenedioxthiopene) coated carbon nanotubes” Analytical Chemistry, 78, 1115 – 1121.

Waldron, A.M., D. Spencer and C. A. Batt, (2006), “The current state of public understanding of nanotechnology” J. Nanopart. Res, 8, 569 – 575.

Zhao, R. X., P. Torley and P.J. Halley, (2008),”Emerging biodegradable materials: starch- and protein-based bio-nanocomposites” Journal of Materials Science, 43, 3058-3071.

Zhou, X., A.L. Porter, D. K. R. Robinson and Y. Guo, (2013), 'Analyzing Research Publication Patterns to Gauge Future Innovation Pathways for Nano-Enabled Drug Delivery' PICMET '13 Conference. "Technology Management in the IT-Driven Services" 28 July – 1 August, 2013: Portland, United States.