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**COMMUNICATION FROM THE COMMISSION TO THE COUNCIL, THE
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COMMITTEE**

**Nanosciences and Nanotechnologies: An action plan for Europe 2005-2009. Second
Implementation Report 2007-2009**

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Nanosciences and Nanotechnologies: An action plan for Europe 2005-2009. Second Implementation Report 2007-2009

Nanotechnology¹ has the potential to enhance quality of life and industrial competitiveness in Europe. The “integrated, safe and responsible approach” proposed by the European Commission (EC) in 2004² has been agreed by stakeholders and is now the core of the European Union’s nanotechnology policy. The Nanotechnology Action Plan 2005-2009³ has provided an impetus for a variety of developments. After the first two years of the Action Plan, progress in almost every area was identified in the First Implementation Report.⁴ This report covers actions undertaken and progress made during 2007-2009 in relation to the key areas identified in the Action Plan. Where appropriate, for the sake of completeness and continuity, developments in preceding years are included. In this Staff Working Document detailed information on progress can be found, while the Communication to which it is attached outlines the key developments in each policy area of the Action Plan, identifies current challenges, and draws conclusions relevant to the future European nanotechnology policy. This document follows the headings of the Action Plan (apart from the last one, on coordination, which is dealt with only in the Communication). International cooperation is now an integral part of the Commission’s policy in all areas of the Action Plan, and is dealt with mainly under the respective policy areas.

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¹ In this report, “nanotechnology” is used as short for nanosciences and nanotechnologies. Although several definitions exist, as a working definition used here, nanotechnology is the understanding and control of matter and processes at the nanoscale, typically, but not exclusively, below 100 nanometres in one or more dimensions, where the onset of size-dependent phenomena usually enables novel applications.

² *Towards a European Strategy for Nanotechnology*, COM(2004)338;
<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2004:0338:FIN:EN:PDF>

³ *Nanosciences and nanotechnologies: An action plan for Europe 2005-2009*, COM(2005)243; hereafter “Action Plan”;

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2005:0243:FIN:EN:PDF>

⁴ *Nanosciences and Nanotechnologies: An action plan for Europe 2005-2009. First Implementation Report 2005-2007*, COM(2007)505;

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2007:0505:FIN:EN:PDF>

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1. RESEARCH

Bringing together public and private organisations across Europe to perform collaborative research and development (R&D) in nanotechnology is vital for the interdisciplinary approach often needed for nanotechnology, as well as for optimising resources. The Action Plan called for nanotechnology R&D to be reinforced and coordinated, and also for synergy with education and innovation to be pursued, in order to generate the “triangle of knowledge” needed for the European Research Area of knowledge for growth. This is the general strategy pursued in the successive Research Framework Programmes (FPs).⁵ Given the diversity of the underlying scientific approaches and the applications in many different sectors, a wide range of research topics have been pursued in the last five years or so. This chapter presents information on European and worldwide funding; describes the different fields of research pursued, including the research on risk assessment; and links this work to industrial needs identified by several European Technology Platforms relevant to nanotechnology. There are also sections on the results from the recent EuroNanoForum conference; and the international cooperation activities. The next two chapters, on infrastructures and human resources, present the complementary activities needed to support innovation.

1.1. R&D Funding

Support for nanotechnology R&D came from both the Framework Programmes and the EU Member States, with particular emphasis on coordination of policies, programmes and projects. Under the 6th Research Framework Programme (FP6, 2002-2006) funding of almost EUR 1.4 billion was provided to more than 550 projects in nanotechnology. By way of comparison, the EC contribution was about EUR 120 million in FP4 (1994-1998) and EUR 220 million in FP5 (1998-2002). Over its lifetime, FP6 accounted for almost a third of total public expenditure on nanotechnology in Europe.

Table 1 Nanotechnology research funding in FP6 (2003-2006) by thematic priority or activity

| FP6 Thematic Priority / Activity | EU funding, M€ | % of total |
|----------------------------------|----------------|------------|
| NMP | 575 | 41.9 |
| IST | 466 | 33.9 |
| Marie Curie ⁶ | 161 | 11.7 |
| Health ⁷ | 57 | 4.2 |
| Infrastructures ⁸ | 40 | 2.9 |
| NEST ⁹ | 24 | 1.7 |

⁵ Framework Programmes of the European Community for research, technological development and demonstration activities – general information at <http://cordis.europa.eu/>

⁶ Specific programme “Structuring the European Research Area”, “Marie Curie Actions - Human resources and mobility”

⁷ Thematic priority “Life sciences, genomics and biotechnology for health”

⁸ Specific programme “Structuring the European Research Area”, “Research Infrastructures”

| | | |
|-------------------|--------------|------------|
| SME ¹⁰ | 17 | 1.2 |
| Others | 33 | 2.4 |
| TOTAL | 1,374 | 100 |

The period 2007-2009, which is covered by the present report, coincided with the first three years of the 7th Research Framework Programme (FP7, 2007-2013). Whilst final figures for 2009 are not available at the time of writing, the Community funding committed following calls in the first two years of FP7, 2007 and 2008, was EUR 1.1 billion. In a way analogous to FP6, this funding came from a number of different themes, with the dedicated NMP theme (Nanosciences, Nanotechnologies, Materials and new Production Technologies) accounting for just over 50 % and the ICT theme (Information and Communication Technologies) accounting for a further 20 %.¹¹ Further contributions came from the “People” and “Ideas” specific programmes, which do not target particular areas or applications.¹² As predicted in the previous implementation report, much of this funding came from the cross-thematic approaches developed in FP7, as nanotechnologies have an interdisciplinary and enabling character and can contribute to different industrial sectors and policy objectives in health, food, environment, energy and transport.

Table 2 Nanotechnology research funding in FP7 (2007-2008) by theme or programme

| FP7 Theme / Programme | EU funding 2007, M€ | EU funding 2008, M€ | EU funding 2007-08, M€ |
|-----------------------------|---------------------|---------------------|------------------------|
| NMP | 282 | 314 | 596 |
| ICT incl. FET ¹³ | 148 | 26 | 174 |
| ENIAC ¹⁴ | 0 | 32 | 32 |
| Marie Curie (People) | 74 | 51 | 125 |
| ERC (Ideas) | 18 | 61 | 79 |

⁹ Specific programme “Integrating and Strengthening the European Research Area”, “New and Emerging Science and Technology”

¹⁰ Specific programme “Integrating and Strengthening the European Research Area”, “Specific SME activities”

¹¹ It should be noted that the overall figure and the share of ICT would have been higher, were it not for the fact that the ICT Work Programme did not include topics in nanoelectronics in 2008.

¹² Despite the fact that these programmes do not target particular areas or applications, the interest in nanotechnology is such, that a sizeable share of the available funding, of the order of 10 %, is allocated to relevant projects following the proposal evaluations. This trend is expected to continue.

¹³ Future and Emerging Technologies objective

¹⁴ ENIAC Joint Undertaking – see section 1.2.1; the figure of EUR 32 million from FP7 was complemented by a further EUR 58 million from the ENIAC Member States, bringing the total public funding to EUR 90 million.

| | | | |
|------------------------|------------|------------|--------------|
| Health | 23 | 14 | 37 |
| Energy | 17 | 20 | 37 |
| Infrastructures | 1.5 | 27.7 | 29 |
| SME | 12 | 7 | 19 |
| Food and biotechnology | 0 | 2 | 2 |
| Science in society | 0 | 1.3 | 1.3 |
| TOTAL | 576 | 556 | 1,132 |

It is interesting to follow the evolution of industrial participation in nanotechnology projects supported by the NMP theme: In the nanotechnology projects selected in the period 2007-2008, industry accounted for 40 % of all participations.¹⁵ As was reported in the previous implementation report, the industrial participation in nanotechnology projects (within the NMP thematic priority of FP6), had risen from 18 % in 2003-2004 to 37 % in 2006. This shows the gradually increasing interest of industry in the nanotechnology topics included in this theme, although inevitably this is still lower than in NMP projects that do not involve nanotechnology (where industry accounts for 57 % of all participations). The industrial participation in nanotechnology projects supported by the ICT theme, which on the whole addresses more mature applications, is higher.

The Commission is also carrying out nanotechnology research directly, through its Joint Research Centre (JRC). The JRC activities span a wide range of nanotechnology areas including nanotoxicology and potential environmental impact; metrology, standardisation and the development and production of reference materials; environmental remediation; and, in the energy area, hydrogen production and storage, and catalysts for fuel cells.

Global expenditure on nanotechnology research, both public and private, in the three-year period 2004-2006 was around EUR 24 billion. Europe accounted for more than a quarter of this worldwide total, with the EU funding directly accounting for 5-6 %. In the two-year period 2007-2008, the global expenditure reached EUR 25 billion. Europe still accounted for about one quarter of the worldwide total. However, in Europe, private funding accounted for only 40 % of the total, whereas in the world as a whole private funding was overtaking public funding (as of 2008).

Table 3 Global nanotechnology research funding (public and private) in 2005-2006 and 2007-2008¹⁶

| Billion € | 2005-2006 | | | 2007-2008 | | |
|-----------|-----------|---------|-------|-----------|---------|-------|
| | public | private | TOTAL | public | private | TOTAL |
| | | | | | | |

¹⁵ These figures refer to participation in individual projects, i.e. counting participations of the same beneficiary in different projects cumulatively.

¹⁶ For the purposes of an approximate global comparison, figures are given in EUR, using 2005 exchange rates. Sources: European Commission and Lux Research

| | | | | | | |
|--------------|-----|-----|-------------|------|------|-------------|
| EU | 3.4 | 1.9 | 5.3 | 3.8 | 2.5 | 6.3 |
| US | 2.8 | 3.1 | 5.9 | 2.6 | 4.1 | 6.7 |
| Japan | 1.5 | 2.4 | 3.9 | 2.7 | 4.4 | 7.1 |
| Russia | 1.5 | 0.9 | 2.4 | 0.8 | | 0.8 |
| China | | | | 0.8 | 0.3 | 1.1 |
| Others | | | | 1.5 | 1.1 | 2.6 |
| TOTAL | 9.2 | 8.3 | 17.5 | 12.2 | 12.4 | 24.6 |

1.2. R&D Domains

This section will discuss the various domains of nanotechnology, that is, nanosciences and nanotechnologies, which are currently addressed by EU-funded research projects. The aim is to give an overview of each domain, outlining expectations, challenges and some results. It should be noted that the rather broad domain of nanomaterials is dealt with under a number of more specific headings. In addition to the projects covered here, other funded projects have addressed risk assessment (treated in the next section); and areas of policy such as outreach, ethics, innovation, metrology and coordination of selected activities (treated in other parts of this report). Finally, projects funded by the “People” and “Ideas” specific programmes are often in fundamental nanosciences, and thus complement to some extent the application-oriented domains described here. Also complementing the domains described here are the activities of an FP6 ERA-NET and an FP7 ERA-NET Plus¹⁷ on nanosciences, NanoScience-Europe,¹⁸ with a current consortium of 17 national funding agencies in 12 different countries.

1.2.1. Nanoelectronics

Nanoelectronics refer to the application of nanotechnology to semiconductor components and highly miniaturised electronic sub-systems, and their integration in larger products and systems. Semiconductors have enabled the digital revolution that has brought huge productivity gains to our economy and improvements in our quality of life. Constant innovation in the area, together with a strong industrial competition, have given rise to affordable, ever more powerful and energy-efficient computers and other digital devices, for the everyday use of all businesses and virtually all types of consumer. The pace of this digital revolution is still accelerating, enabling new applications in nearly every segment of the world economy, such as medical devices, photovoltaic energy generation, traffic management, and so on.

Current devices are manufactured using 65 nm or 45 nm processes (this dimension being the average half-pitch of a memory cell). In this sense, nanoelectronics is merely the consequence of the evolutionary path of microelectronics into the nanoscale domain. Current transistors still do not fall under the category of nanomaterials, which are produced by manipulating

¹⁷ The objective of the ERA-NET scheme is to support the coordination of national and regional research programmes. In the case of ERA-NET Plus, there is additional EU funding of a joint trans-national call, up to 1/3 of the total.

¹⁸ <http://www.nanoscience-europe.org/>

matter at the atomic scale. On the other hand, the properties of future devices may well be defined by interatomic interactions and quantum mechanical properties.

The first generation of CMOS (complementary metal-oxide semiconductor) chips were based on a lithographic process with features inside the transistors of 10 micrometres or more. The chips in most products in use today have lateral features more than a hundred times smaller – just 90 nm or 65 nm, approximately a thousand times smaller than the width of a human hair. That may be small, but in the competitive semiconductor industry, where size is crucial, it is not small enough.

A reduction in minimum feature size means more transistors per chip, more transistors means more computing and processing power, and more power means more performance and more functional electronic systems: PCs, mobile phones, vehicles, satellites, and so on. And, because the processed silicon wafers out of which chips are made are increasingly expensive (setting up a factory to produce them today costs EUR 3 billion), smaller dimensions also make it possible to use fewer of them to do more, meaning that reductions in device cost can continue.

The continuous miniaturisation of the current transistors is approaching its physical limits, however, and disruptive approaches are needed to maintain this trend. Current transistor candidates for future technologies are significantly different from traditional transistors and fall entirely within the realm of nanotechnology. Some of these candidates include hybrid molecular and semiconductor electronics; one-dimensional nanotubes and nanowires; and advanced molecular electronics. Although all of these hold promise for the future, they are still under development and are unlikely to be used for manufacturing in the near future.

In 2007 and 2008, about EUR 106 million was dedicated to R&D projects in the area of nanoelectronics – this includes projects under the Future and Emerging Technologies (FET) objective.

ENIAC is the European Technology Platform (ETP) dealing with nanoelectronics. It is a large-scale, application-driven initiative mobilising all European actors in this innovation- and technology-intensive sector. The Commission identified nanoelectronics as a strategic area where the new funding mechanism of a Joint Technology Initiative (JTI) could be implemented. The ENIAC Joint Undertaking (JU), the legal instrument implementing the industry-oriented part of the Strategic Research Agenda (SRA) of the ENIAC ETP, is active since the beginning of 2007. The ENIAC JU has already launched two calls for proposals.¹⁹ Following the first call in 2007, eight projects are already underway with a total public funding of EUR 90 million (EU and Member States combined). The total public funding for the second call of 2009 was EUR 104 million.

As examples of EU-funded research projects in nanoelectronics, NanoCMOS and PULLNANO are amongst the most significant in terms of research results. The NanoCMOS initiative, which ended in June 2006, developed the technology to create a 45 nm generation (or technology node) of chips. The follow-up project, PULLNANO, is currently working on developing nodes as small as 32 nm and even 22 nm.²⁰ At that diminutive size, semiconductor manufacturing is continuing to test Moore's Law, a prediction made by Intel co-founder Gordon E. Moore in 1965 that the number of transistors that can be cost-effectively placed on a chip will double approximately every two years.

¹⁹ <http://www.eniac.eu/web/calls/callforproposals.php>

²⁰ <http://www.pullnano.eu/> and <http://www.nanocmos.ac.uk/>

Progress has been made in the resolution obtained in top-down structuring of nanoelectronics devices:

- Optical lithography methods – using 193 nm exposure wavelength with liquid immersion (water) and simultaneous application of double exposure – can produce features below 30 nm. It is expected that so-called computational lithography can extend optical lithography even down to 20 nm (from design to mask making and the final exposure of the silicon wafer, all processes are optimised by numerical simulation of the individual steps).
- EUV (extreme ultraviolet) lithography – using 13 nm exposure wavelength – can bring resolution down to 10 nm or less; this could be extended by changing to even shorter EUV exposure wavelengths of 5 nm to 7 nm.
- Multi-e-beam maskless lithography is envisaged, with relatively high wafer throughputs (5 to 10 wafers per hour). This has the advantage of avoiding extremely expensive mask making, which is of interest only for low and medium-volume production of application driven semiconductor components (rather than commodity products). Here resolutions in the 10 nm to 20 nm range have been demonstrated. Introduction into industry is expected in the next two to four years.

Nanoimprint technology is not considered here, as it is limited to applications where only one mask level is sufficient to make a product (e.g. magnetic heads). The reason for this is that the template allows only a one-to-one pattern transfer in contact with the substrate.

Extreme resolutions have been obtained recently with bottom-up techniques:

- Electron Beam Induced Deposition (EBID) using a scanning transmission electron microscope (STEM): A group at the TU Delft, in cooperation with Arizona State University, have “written” tungsten-containing dots with an average diameter of 1 nm, thereby setting a new world record and probably a limit for EBID. This method is based on surface adsorbed molecules which dissociate into volatile and non-volatile parts under the influence of an e-beam; the non-volatile parts stick to the substrate where they have been dissociated, while the volatile ones are pumped away.
- Molecular self-assembly using DNA nanotechnology, e.g. to make DNA nanotubes. The DNA is used as a structural material rather than as a carrier of genetic information, making this an example of nanobiotechnology. Apart from flat sheets, arrays have been made to form hollow tubes of 4-20 nm in diameter. These DNA nanotubes are somewhat similar in size and shape to carbon nanotubes, but are more easily modified and connected to other structures.

In Europe, there are four main regional clusters active in nanoelectronics. These clusters combine the expertise of companies, training centres and public or private research units in a given geographical area, and are committed to generating synergies within common innovation projects. These are in the areas of Grenoble (ST, CEA-LETI), Dresden (Infineon, AMD, CNT) and the Leuven-Eindhoven-Aachen triangle (NXP, IMEC); and the emerging Irish cluster around Intel Ireland.

1.2.2. Nanophotonics

Photonics is used more and more in core as well as in access networks. Photonics is also an enabling technology that exploits advances in lasers, light sources, fibres and detectors; in materials (e.g. nanotubes, nanocrystals and organics); and in architectures and manufacturing processes (hybrid integration, silicon photonics and CMOS compatibility). It promises to play a major role in new areas such as energy conservation (e.g. by improving photovoltaic and lighting efficiency), medicine, biology, environment and safety. The possibility to

manufacture structures at the nanoscale – well below the wavelength of light – will radically change traditional approaches, by exploiting physical effects not previously accessible. Europe has strong and recognised R&D capabilities, as well as SMEs, in photonics.

- The MONA project (Merging Optics and Nanotechnologies) was launched in June 2005 to bridge the gap between photonics and nanotechnologies. Its ultimate objective was the development of a European roadmap for nanophotonics. This roadmap identifies key nanomaterials having the strongest impact for nanophotonics (such as quantum dots and wires) and also covers the integration of electronics and photonics.

1.2.3. Nanomedicine

Nanomedicine is the application of nanotechnology to health. It can improve quality of life by enabling true preventive medicine and precisely targeted intervention, as well as regenerative therapy. Nanomedicine works on the basis of producing man-made functional structures matching the typical size of natural biological elements, to achieve more effective and specific interactions. This approach has much potential for breakthroughs in basic, applied and clinical sciences, leading to more efficient and targeted diagnosis, treatment, and monitoring of disease. This is relevant to the treatment of a wide variety of diseases from cancer to diabetes; cardiovascular, immunological, inflammatory, musculoskeletal and neurodegenerative disorders (Alzheimer's and Parkinson's diseases); and infectious diseases. It can moreover enhance competitiveness by creating jobs with high added value; and in the longer term by reducing social care costs and leading to affordable healthcare for an ageing population.

The Nanomedicine ETP has identified three areas of industrial priority in nanomedicine research: diagnostics including medical imaging; targeted drug delivery; and regenerative medicine. These are described in separate sub-sections below.

The NMP, Health and ICT themes are all involved in the funding of nanomedicine projects. EU funding for nanomedicine was around EUR 330 million in FP6 (2002 – 2006) and EUR 280 million in the first two years of FP7 (2008-2009).

There is also an ERA-NET in nanomedicine, EuroNanoMed,²¹ which serves as a platform to launch joint calls in nanomedicine, with the participation of 18 states and regions. The first joint call for transnational projects closed in September 2009.

Ethical, legal, social, and regulatory aspects are of particular importance for the successful development of nanomedicine. There are therefore several EU-funded support actions to address these issues (e.g. NanoMed Round Table).

Devices and nanomaterials used in nanomedicine need to be biocompatible and their fate needs to be known, both *in vivo* and *ex vivo*. In this respect, the toxicology of nanomaterials is also very important.

1.2.3.1. Diagnostics including medical imaging

Diagnostic technologies, including medical imaging based on nanotechnology, have the potential to permit earlier diagnosis and therapy for a wide range of diseases, reducing risks for the patient and allowing less severe and less costly treatment. The area can be divided into *in vivo* and *in vitro* diagnostics, the goal in both cases being to detect an evolving disease as early as possible, ultimately up to the point of detecting single cells or biomarkers indicating the onset of a disease. Of interest in the area of *in vitro* diagnostics is a trend towards “point-

²¹ <http://www.euronanomed.net/>

of-care” diagnostics, allowing a sample to be analysed by the doctor or the patient, without the need for a central laboratory.

Early diagnostics are based on the identification of disease-related biomarkers, which could offer an earlier and more personalised assessment before the onset of symptoms. Nanotechnology can help achieve early diagnostics, for example by making use of highly sensitive *in vivo* and *in vitro* tests capable of identifying disease-specific molecules present in a sample.

In connection with medical imaging, nanotechnology allows the development of improved, targeted contrast agents providing a better identification of diseased tissues, for instance with X-ray or magnetic resonance imaging (MRI). Molecular imaging, based on the use of specific targeted contrast agents, plays a crucial role in the non-invasive localisation of a disease, minimising discomfort and pain for the patient.

Related to diagnostics, is the idea of targeting the therapy to a biological function which is specifically altered in a certain disease (often called “theranostics”). With this strategy, the tissue of interest can firstly be imaged, using target-specific contrast nanopharmaceuticals. Then, combined with further pharmacologically active agents, or with other stimuli (e.g. laser light), the same targeting strategy can be used for applying the appropriate therapy. Finally, the monitoring of the effects of treatment is possible by further sequential imaging.

Examples of relevant projects include:

VIBRANT: Around 30 million people in Europe currently suffer from diabetes, with an incidence of 7.5 % in Member States. This devastating disease is ranked among the leading causes of fatal cardiovascular diseases, kidney failure, neuropathy, lower limb amputation and blindness. At present, no clinically established methodology exists for non-invasive *in vivo* imaging and quantification of insulin-producing beta-cells in the pancreas, whose dysfunction is responsible for diabetes. VIBRANT proposes a new nanotechnology-based method for the MRI imaging of beta-cells. Furthermore, target-specific drug-loaded nano-containers will offer high potential for cell-directed therapies.

CAREMAN: Diagnostic devices based on biosensor technology coupled with detection capabilities and integrated sample handling aim to tackle the most common diagnostic problems currently faced in EU hospitals – such as cardiovascular diseases, coagulation disorders, chronic and acute inflammation, cancer and thyroid disorders. The innovative solutions that these devices introduce may lead to the eventual replacement of traditional diagnostic techniques.

1.2.3.2. Targeted drug delivery

Targeted drug delivery systems selectively transport drugs to diseased cells and tissue, thereby minimising the negative side-effects of these drugs in other areas of the body. Effective drug delivery is one of the biggest challenges in pharmaceutical research.

Therapeutic entities can be small molecules, but also proteins, antibodies, nucleic acids, antigens, peptide mimics, and so on. Delivery systems should have a significant therapeutic payload. The efficient administration of a compound relies on the ability to reach the intended target, for example to cross the blood-brain barrier in treating neurological diseases. The method of administration is also important, as it plays an important role on biodistribution, exposure, safety and efficacy.

A range of emerging technologies address delivery needs, for example the encapsulation of the active compound in functionalised nano-vectors, or the external direction and release of a

drug using magnetic nanoparticles. In all cases, the target must be identified by discovering and validating new biomarkers on the basis of molecular recognition.

Nanopharmaceuticals and nanodevices can also be activated by external means (magnetic resonance imaging, focused ultrasound, radiotherapy or lasers), in order to deliver an intended physical effect in a localised or systematic way. This effect could be heat or radiation to kill tumour cells. Alternatively, the external means can be used for the localised release of a drug at predetermined levels.

Examples of relevant projects include:

ASMENA: The development of new medicinal products is currently hindered by difficulties related to the reliability and efficiency of screening membrane proteins as candidate drug targets, despite their constituting more than 50 % of all drug targets. A new nanotechnology, combining nano-porous substrates and proteoliposome self-assembly, promises to deliver a sensor chip to quantify screening assays of drug candidates that may be suitable for commercial application.

SONODRUGS: By allowing drugs to be delivered to disease sites via the patient's bloodstream and then activated by focused ultrasound pulses, the project aims to maximise the therapeutic efficiency and minimise the side effects of drug treatments for cancer and cardiovascular disease. The project's research on MRI-guided drug delivery will focus on potential treatments for cancer. It aims to develop MRI techniques that simultaneously image the patient's anatomy, detect the arrival of MRI-labelled drug-loaded particles at the disease site, measure the local heating effect of the ultrasound pulses, and monitor the temperature-triggered release of drugs from the particles.

NANOEAR: This project aims to develop therapies for inner ear disorders, using novel multifunctional nanoparticles that are targetable to selected cell populations for controllable drug release.

1.2.3.3. Regenerative medicine

A broad definition of regenerative medicine includes the repair, replacement and regeneration of damaged tissues or organs (e.g. skin, muscle, nerves, cardiac tissue etc), with the use of approaches that can roughly be divided into two overlapping areas: smart biomaterials and advanced cell therapy. Therapies based on tissue engineering represent a breakthrough in regenerative medicine, through the use of intelligent biomaterials, smart implants, and cell-based techniques.

The focus of regenerative medicine is to stimulate tissue regeneration and repair by using the body's self-repair mechanisms. This process can use adult, endogenous stem cells. Smart nanostructured or nanopatterned biomaterials can serve as scaffolds, stimulating the regeneration process by providing the necessary signalling molecules to the cells to start regenerating a particular tissue.

Examples of relevant projects include:

NANOSCALE: Understanding the physical and chemical events at the nanoscale, which occur during the interaction of several cell types (including neurons and stem cells) with nanostructures, is of paramount importance for the fabrication of biocompatible surfaces to induce stem cell proliferation and differentiation, and to guide neuronal growth.

TEM-PLANT: This project aims to use hierarchical structures that naturally exist in plants, to generate innovative biomedical devices designed for bone and ligament substitution. This

leads to the development of intricate but extremely functional architectures, which are constantly able to adapt to ever-changing mechanical needs.

1.2.4. Converging sciences and technologies; nanobiotechnology

Nanobiotechnology is a broad field of knowledge and techniques, involving the convergence between nanotechnology and the basic components of life: proteins, DNA and cells. The interface of these fields has the potential to provide revolutionary scientific and technical approaches to address existing and new applications. This large domain has inevitable overlaps with other domains discussed in this section, particularly with nanomedicine and self-assembly.

Nanobiotechnology is based on the fact that biological systems and processes within the cell operate at the nanoscale. Functional biological units, such as proteins, are to be found at the nanoscale; while cells are much larger, at 10 to 100 micrometres. One striking fact about biology is that organisms are built following the bottom-up approach. For instance, proteins are built by putting together molecular building blocks called amino-acids, according to a “plan” encoded in the DNA of the cell. Amongst the most innovative nanomedicines currently under development are nanostructures functioning as release systems for completely synthetic oligonucleotides.

Like nanotechnology, nanobiotechnology is a strongly interdisciplinary field (the term bionanotechnology is often used in the same sense). It includes two approaches: On the one hand, we try to learn about nature, so that we gain insight into biological processes, which have very important applications in medicine (nanomedicine) and biotechnology (food, industrial applications and environmental monitoring). On the other hand, we try to learn from nature, so that we can build useful systems at the nanoscale, using processes similar to those optimised by nature over millions of years. Contrary to popular belief, it is impossible to make conventional machines at the nanoscale, for a number of fundamental reasons. Nevertheless, one can build nanostructures and “devices” of certain kinds by imitating nature.

Molecular motors could eventually be built using certain biological molecules as building blocks. These could be used to make sorting devices for molecules, or in developing nanoscale manufacturing. For example, the Hy3M project (Hydrogen-bond geared Mechanically Interlocked Molecular Motors) created new types of synthetic molecular motors – fuelled by energy in the form of light, heat or electrons – which transmit the effects of mechanical motion from the molecular level through to the macroscopic world.

Nanobiotechnology is expected to provide innovative tools, for example, sensors to analyse biological samples; label and track single molecules or trace elements; and improve the fabrication of novel nanostructured materials (biomimetic materials), leading in turn to better fuel cells, solar cells and filtration membranes.

As discussed in the relevant sub-section above, developments in nanobiotechnology can be brought together in the field of nanomedicine, the application of nanobiotechnology to health. Another emerging area of relevance for nanomedicine is the convergence of biological, information and cognitive sciences. One example is the interface between nanoscale systems, neurons and the brain, which is important for the development of intelligent brain-controlled prostheses, such as arms, legs, hands, ears and eyes. Even though this area is not considered to be of immediate industrial relevance, it has been addressed by some EU-funded projects (e.g. NEURONANO, SMARTHAND, DREAMS and NANOBIOACT).

The 2009 Work Programmes of KBBE (biotechnology and food) and NMP included five coordinated topics on nanobiotechnology, which were met with an excellent response: Smart devices to study biomolecular dynamics in real time; functionalised membranes; bio-

interfaces for environmental applications; applying life science principles as model for new nanotechnology-based mechanisms, processes, devices or systems; and analysis of the ethical, safety, regulatory and socio-economic aspects.

1.2.5. Self-assembly and directed assembly

A large and diverse area of research involves the development of nanostructures with controlled physical properties. Such nanostructures can have a significant impact in energy and environmental applications, nanoelectronics and photonics, nanomedicine, catalysts for the chemical and pharmaceutical industry, and so on. Environmentally sustainable growth can result from a more efficient use of materials and energy, and from cleaner transport.

Self-assembly essentially involves interactions at a higher level and lower strength than standard chemical bonds, forming structures with an ordering beyond that of their individual components, i.e. nanostructures. Closely related to self-assembly is the concept of self-organisation. One can distinguish between processes where the building blocks carry specific information directing the self-assembly through recognition; and processes based on templated growth methods, where building blocks are deposited onto pre-patterned substrates and their assembly is directed by the pre-existing pattern. These processes may in addition be assisted by external factors such as electromagnetic fields, fluid flow or other boundary conditions.

Directed self-assembly, frequently combined with more traditional “top-down” approaches, allows one to create nanostructures with a set of desired and controllable properties. The control of the process and the characterisation of the resulting structures are the usual challenges in this field. In the longer term, it is desirable to find ways of “up-scaling” such processes, to make them industrially relevant. In addition to scale, uniformity is an important consideration in up-scaling. Several projects have been or are being funded in this broad area, with mixed results: Often, the particular applications pursued by a project turn out to be impossible; on the other hand, valuable new methods for the synthesis, modelling and characterisation of materials are being developed. The industrial participation in such projects has tended to be peripheral, but is growing.

Projects currently selected for funding in this area generally have an increased focus on realistic applications, although the production scale remains a challenge. In 2009, this activity was complemented by a call topic on molecular manufacturing, that is, engineering functional structures at the molecular scale to achieve sub-micro, micro- or macro-scale objects, possessing controlled properties over multiple scales. An important aim of this topic was to stimulate the industrial take-up of novel nanotechnology-based solutions within existing or new production lines.

1.2.6. Tools for nanosciences and nanotechnologies

While nanoscience is not entirely new, since the invention of the Scanning Tunnelling Microscope (STM) and the Atomic Force Microscope (AFM) in the 1980s, researchers have developed increasingly powerful techniques for “seeing” and controlling objects, surfaces and structures at the nanoscale. Most applications in nanotechnology discussed elsewhere in this section became possible after that, highlighting the importance of developing appropriate instruments for material characterisation. Furthermore, the development of instruments is in itself an important area of innovation, especially for SMEs.

Researchers continue to develop techniques to measure and characterise novel materials and effects at the nanoscale. Several projects funded under FP6, as well as in the first calls of FP7, have addressed this area. Relevant topics included “Pilot lines to study, develop and up-scale nanotechnology-based processes from laboratory”; “Equipment and methods for

nanotechnology”; “Specific, easy-to-use portable devices for measurement and analysis”; and “Pilot lines to introduce nanotechnology-based processes into the value chain of existing industries”.

The Nanobeams Network of Excellence concentrated on analytical techniques using focused ion and electron beams in order to develop analytical techniques and instruments matching the requirements of nanomaterials. This network combined the efforts of manufacturers of scientific instruments with those of leading research laboratories in the field.

Relevant projects selected under FP7 include several examples where combinations of atomic-scale characterisation technologies introduce new capabilities, such as the following:

- 3D NanoChemiscope: 3-dimensional chemical characterisation of nanostructured inorganic and organic materials with lateral resolution down to 10 nm or less and depth resolution down to 1 nm;
- FIBLYS: Probing of electron-matter interactions, e.g. detection of electron-beam induced current, or cathodoluminescence phonons, or backscattered electrons directly at the surface – with nanoscale resolution;
- MDSPM: Imaging of metallic, semiconducting and insulating surfaces with unprecedented resolution, expected to improve our understanding of entire areas of surface science such as chemical reaction dynamics, local energy dissipation and excitations, nanoscale contacts and a rational approach to catalyst design, to name a few;
- SMW: Combining three advanced microscopic techniques into a single workstation for reaching a new quality level in the study of the correlation between structure and function of living cells, with applications in immunology and cancer research; and
- Nano DNA sequencing: Sequencing of single molecules of genomic DNA in a number of hours, much faster than current conventional techniques, and possibly detection of different types of DNA based on their electrical properties.

Inspection and monitoring systems for security is another important area addressed, exemplified by current research projects:

- TeraEye: Scanning systems detecting harmful materials based on passive THz detection, supporting a radical transformation in the security sector; and
- Dynamics: Nano-biological sensing for detection of biological threats, and environmental assays using a lab-on-a-chip device that will be able to detect pathogens in water.

1.2.7. Industrial applications, including pilot lines

Significant investments have been made throughout FP6 in long-term research in various fields of nanoscience. In many cases, these projects have produced results in the laboratory environment (for example in terms of desired properties), but the transfer of promising nanotechnology research results into new industrial technologies still represents a bottleneck.

In order to accelerate the introduction of nanotechnology-based products into markets and to stimulate the development of the European nanotechnology industry, the NMP theme has invited proposals for “Nanotechnology Pilot Lines” in the first two calls of FP7. The projects are expected to focus on the development of innovative nanotechnology-based processes to pilot-line scales, in order to improve industrial processes and production lines. The projects are also expected to demonstrate how nanotechnology can significantly improve the value-chain in industrial production towards high-added-value innovative products, thereby enhancing European competitiveness.

The calls have been met with a good response from both the research and industrial communities. Seven projects have been funded, with EUR 50 million. A further two pilot-line projects have been funded in the Production Technologies area of NMP, with EUR 19 million, bringing the EU contribution to pilot lines to EUR 69 million (with a total investment of EUR 98 million). Collectively, these nine projects have over 150 participants, including 30 large industrial partners and 43 SMEs, making the industrial participation close to 50 %. Technology demonstration is a significant component of these projects, with nearly a quarter of the effort dedicated to demonstration activities. To allow sufficient time for technology demonstration, most projects will run for four years. Safety and life cycle assessment are also taken into account.

As the objective of the pilot-line calls has been to support the progress of the most promising laboratory results towards industrial applications, they were not designed to be sector- or application-specific. As a result, they cover a wide range of applications and processes:

- Electrochromics for shading appliances;
- Atmospheric plasma deposition for nanoscale industrial surface processing;
- Atmospheric pressure plasma processing for 3D nanostructured surfaces;
- Nanopatterning based on nanoimprinting lithography;
- Antibacterial and antifungal medical textiles;
- Scale-up of the incorporation of nanoparticles in papermaking;
- Functional magnetic nanoparticle separation;
- Production of nanofluid coolants; and
- New generation of fluid lubricants incorporating nanomaterials.

A holistic approach is common for the projects covering, for example, (i) development of scalable nanomaterial production technologies; (ii) development of large-scale processing technologies that can be used with the produced nanomaterials; and (iii) technology integration and pilot-scale demonstration of real, industrial applications. Ensuring the safe production of nanomaterials, as well as the safety of the final application or product, forms an integral part of the projects.

The pilot-line projects are expected to result in significant improvements in productivity, sustainability, product quality and its control; and to demonstrate the economic viability of the use of nanotechnology in their respective application areas. As the projects are at a very early stage of implementation, it is premature to anticipate the results.

Apart from the dedicated pilot-line calls, several other projects target industrial applications: for example, CANAPE on the production of carbon nanotubes; AMBIO on nanostructured surfaces to control bio-fouling; and INDOT on the production of nanophotonic devices.

Turning to the general outlook for industrial applications, the second half of FP7 is expected to see a gradual shift towards more application-oriented research, as nanotechnologies developed in a laboratory environment evolve towards applications in various industrial sectors. A shift is also expected towards call topics that are more specific to particular sectors or technologies, as part of the effort to generate critical mass and more strategic impact for selected application fields of high priority. The potential for nanotechnology-enabled industrial applications in different sectors is outlined in section 4.3.

1.2.8. Applications in energy and environment

Nanotechnologies have a significant potential for breakthrough advances in sustainable energy conversion processes, addressing in this way current environmental and climate change challenges.

The 2009 Work Programme of NMP included a call “Nanotechnology for harvesting energy via photovoltaic technologies”, with the objective of supporting innovative scientific and technical research for improved efficiency, bringing devices with a more favourable cost per unit-area. The call was met with an excellent response: 70 proposals addressed a wide variety of nanotechnology-based materials and approaches for increasing the efficiency of solar harvesting.

The vast majority of commercial solar cells today is based on crystalline silicon, because of the high module efficiencies that can be achieved. Yet the technology is rather expensive. A sizeable number of the proposals therefore focus on solving this issue through alternative approaches using silicon, significantly reducing the cost without compromising the cell efficiency. Another popular topic was the enhancement of the performance of second-generation thin-film cells, while maintaining low production costs. The proposals typically take into consideration the scaling-up of the laboratory results, as well as the construction of prototype cells with the help of industrial partners, for a realistic proof of concept and eventual industrial take-up. There is good reason to believe that the funded projects will pave the way for highly efficient photovoltaic cells with costs well below the “\$1-per-Watt” benchmark.

Complementary to the call on photovoltaics, the 2010 Work Programme of NMP includes a topic on thermoelectric energy converters based on nanotechnology. Such converters could find applications in transport, power generation and refrigeration requiring a high power output. For example, in vehicles using internal combustion engines and power generation plants, waste heat could be recovered, leading to cost savings and environmental benefits.

Water treatment, whether for the production of drinking water or for the decontamination of polluted water, makes ample use of membrane filtration and of catalytic oxidation or reduction. The use of nano-engineered or nanostructured materials can significantly enhance the efficiency and selectivity of these processes (through process intensification and reduction of by-product generation), and reduce their energy consumption (through lower pressure drops). This leads to a much greater cost-effectiveness, and can also help with the production of portable water-treatment equipment.

- CLEANWATER aims to develop photocatalytic active membranes capable of exploiting solar energy for improved detoxification of water streams (targeting cyanobacterial toxins, pesticides and endocrine disrupting compounds).
- MEMBAQ aims to mimic the selective transport of water through plant leaves by incorporating the plants’ selective channel structures, aquaporins, in polymer membranes.
- MONACAT aims to produce flow-through catalyst units for the reduction of nitrates, bromates, and perchlorates, and for the oxidation of a range of organic pollutants including pesticides and endocrine disruptors.
- NAMETECH aims to enhance the permeability and stability of membranes for water treatment, while reducing their vulnerability to fouling, by incorporating nanoparticles and nano-engineered materials.
- NEW ED aims to develop nanoporous bipolar membranes for the remediation of highly saline industrial waste water streams through electro dialysis.

- WATERMIM aims to produce highly selective “molecularly imprinted” membranes, by first introducing and then removing target substances, so that these membranes are structured with nanosized pores that will preferentially absorb target substances.

1.2.9. Catalysts

Catalysts play a major role in the chemical industry and other related industries, being the basis for more than 20 % of the world’s industrial production processes. Catalysts are key factors in minimising demands on energy and raw materials, as well as in reducing emissions from industrial chemical production. Since many basic chemicals are produced via catalytic routes in volumes exceeding one million tonnes per year, even minor improvements in catalyst performance translate into large savings in raw materials and energy consumption in large-scale processes. Given the fact that the European chemical industry is a major player in catalysis, activities in this field are a key to European competitiveness.

The high surface-to-volume ratios (specific surface areas) of nanomaterials makes catalysis one of the principal ways in which they can contribute to sustainable manufacturing. Nanomaterials can be particularly effective as catalysts, leading to reductions in raw material and energy costs, improvements in selectivity and the minimisation of waste streams in many industrial processes. Using nanomaterials also allows reductions in the required amounts of precious metals, such as platinum and palladium, which are extensively used as catalysts.

Given the large range of applications that oxides have in catalysis and surface chemistry, it is not surprising that nanostructured oxides²² can have a significant impact in fields like the production of petrochemicals (e.g. reforming of light hydrocarbons), intermediates and fine chemicals, with the benefits described above. There are further benefits in environmental protection, for example in the abatement of NO_x, SO₂ and VOCs (volatile organic compounds). It is estimated that by 2020, nanostructured oxides will represent about one third of the total demand for metal oxides (including catalysis and other applications), from slightly more than 1 % today.²³ Last but not least, nano-catalysts are expected to have an impact in biocatalysis, such as the use of biomass, the production of biofuels, and the further development of an integrated and diversified biorefinery that can handle various feed stocks.²⁴

1.3. Research on health, safety and environmental issues (HSE)

It is necessary to understand any risks posed to human health and the environment by nanomaterials, and more generally products based on nanotechnology, and to develop appropriate testing methods and exposure measurements, including equipment. This section describes only the research aspects of risk assessment, while chapter 6 presents the overall picture with regard to health, environmental and consumer protection, including the regulatory aspects.

²² New compound oxides containing non-transition metals, such as doping TiO₂ with anions such as (carbon and nitrogen are not anions), SnNb₂O₆ or BiVO₄ for direct hydrogen production through photocatalysis; Ni-catalyst based on a Mg-Al-Spinel with a high activity and resistance to sulphur for catalytic reforming of light hydrocarbons; and so on.

²³ V. Cortés Corberán & J. Carlos Conesa (2006), The Concorde NSOCRA White Paper – A Technology Roadmap on NanoStructured Oxide Catalysts for Redox Applications, SOCINTEC-Grupo AZERTIA – CONCORDE Consortium, May, ISBN 84-933135-4-8, Coordinated Action under FP6 – Contract Nr. NMP2-CT-2004-505834; K. Walsh (2007), Strong Economy and New Chemical Capacity Drive Demand, February 14/21, pp. 24, www.chemweek.com; R. Coons (2009), Catalysts: Seeking the Next Big Thing, Chemical Week, May 4, pp. 19-21, <http://www.chemweek.com>

²⁴ R. Coons (2009), Catalysts: Seeking the Next Big Thing, Chemical Week, May 4, pp. 19-21, www.chemweek.com; ICIS Chemical Business (2009), Catalyst creativity – Innovative catalysts promise to improve the economics of chemical production, May 4-10, pp. 28-29, <http://www.icis.com>

Since 2005, the EU Scientific Committees have highlighted in their opinions the paucity of information in areas that are fundamental to the further development of guidelines on the risk assessment of nanomaterials. These are:

- (1) Information on nanomaterials on the market;
- (2) Methods with comparable, reproducible and repeatable results;
- (3) The choice of the most appropriate metrics for hazard and exposure assessment;
- (4) Actual human and environmental exposure;
- (5) Methods to extrapolate from the toxicology of non-nanoscale materials to nanomaterials; between nanoparticles; and from laboratory tests to actual hazards to humans (including more sensitive groups) and the environment;
- (6) Toxicokinetics of nanomaterials from various portals of entry to target organs, including possible new endpoints;²⁵
- (7) Environmental fate, distribution and persistence (including bioaccumulation and biodegradability), and ecotoxicity of nanomaterials.

Research projects and support actions designed to address the concerns with regard to health and environmental safety (HSE) have been launched with Framework Programme funding, and also by the European Commission's Joint Research Centre (JRC). The funding for HSE research under the EC Framework Programmes has increased significantly over the years. In total, around EUR 75 million has been spent or committed in this area since 2005, of which EUR 50 million was committed in the first two years of FP7 (2007 and 2008) alone. Further research on safety is built into projects developing applications in order to integrate safety aspects at the earliest possible stage, in accordance with the "integrated, safe and responsible" development of nanotechnologies and the Commission's Code of Conduct.²⁶

A compilation of HSE research projects funded by the EC Framework Programmes, EU Member States, and Associated States²⁷ was published in January 2008.²⁸ In April 2008, the Commission organised a workshop on "Research Projects on the Safety of Nanomaterials: Reviewing the knowledge gaps", and published its proceedings.²⁹ In order to set common deliverables and carry out strategic planning, a "nanosafety cluster" was formed in February 2009 for research projects addressing nanotechnology safety. It includes 24 FP7 projects, with five more projects to be added by the end of 2009, and two national projects. The priority areas in this cluster are:

- Standard methods for measurement and characterisation of nanomaterials;
- Behaviour of nanomaterials in the body and in the environment; mechanisms of toxicity;
- Effects of nanomaterials on the human body and the environment; test methods including alternative test methods;
- Models and calculations to predict and assess toxicity, exposures and risks;

²⁵ In the context of toxicity and ecotoxicity, endpoints are properties related to human health and environmental safety. They should provide basic characterisation, fate, ecotoxicity and mammalian toxicity information for nanomaterials.

²⁶ Commission Recommendation on a *Code of Conduct for responsible nanosciences and nanotechnologies research*, C(2008)424; section 5.1 below

²⁷ States associated to FP6 and FP7

²⁸ <ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/final-version.pdf>

²⁹ ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/final_report.pdf

- Database and information needs;
- Fate and behaviour of nanoparticles in the environment; and
- Risk assessment and life cycle assessment.

Coordination in this area is also aided by a new High-Level Group on nanotechnology, of Member States and FP7 Associated States. One objective of the group is to maximise synergy between EC and nationally funded research work, given that national programmes increasingly extend their funding to HSE research. Furthermore, an *ad hoc* industrial advisory group for safety has also been proposed. For the future, the intention is to integrate all stakeholders' dialogues in a European Technology Platform, complemented and assisted by national platforms. These activities are also coordinated with stakeholders and international partners in appropriate forums, such as the OECD Working Party for Manufactured Nanomaterials (WPMN) and ISO.³⁰

These activities have led to an improved understanding of the interaction mechanisms of nanomaterials with biological systems, as well as of the exposure and measurement issues. Progress in key areas of environmental, health and safety research is described in the following sub-sections, while section 6.4 describes aspects of risk management linked to the progress of this research, and section 6.5 outlines further research necessary to close the knowledge gaps.

1.3.1. Characterisation, metrology and reference materials

It is widely acknowledged that a proper characterisation of nanomaterials in terms of a number of key physicochemical properties is essential for a sound comparison of toxicological test results. Work within the OECD-WPMN and ISO/TC 229 has resulted in an initial consensus on a list of properties to be assessed prior to a toxicity test,³¹ comprising the following issues and properties: particle size and distribution; aggregation and agglomeration state; composition; shape; solubility; dispersibility; surface area; surface chemistry (for example hydrophobicity); and surface charge. Testing methods exist for all these parameters, although not all are as yet validated for use with nanomaterials, nor standardised.

It is clear that the physicochemical characterisation of nanomaterials tested for toxicity in various biological media is a challenge in itself. Even between laboratories with adequate equipment and specific expertise there is not always satisfactory reproducibility, because many of the relevant properties strongly depend on the measurement method used to assess them.^{32 33} On the other hand, given the dynamic nature of some of the listed properties, their measurement cannot easily be outsourced and physically separated from the toxicology test. This calls for increased collaboration between physicists, chemists, biologists and toxicologists. This collaboration will necessarily involve stages of round-robin testing to

³⁰ More information on the work in the context of these two international organisations can be found in section 6.6

³¹ Guidance Manual for the Testing of Manufactured Nanomaterials – OECD-WPMN Sponsorship Programme, ENV/JM/MONO(2009)20

³² Interlaboratory Study to Establish Precision Statements for ASTM E2490-09 Standard Guide for Measurement of Particle Size Distribution of Nanomaterials in Suspension by Photon Correlation Spectroscopy (PCS), Research Report E56-1001, ASTM Committee E56 on Nanotechnology, Subcommittee E56.02 on Characterisation: Physical, Chemical, and Toxicological Properties, April 2009

³³ O. Couteau, G. Roebben, *Comparison of dynamic light scattering and centrifugal sedimentation for nanoparticle sizing*, Euronanoforum 2007, Nanotechnology in Industrial Applications, June 19-21, 2007, Düsseldorf, Germany

assess the proficiency of laboratories and reproducibility of methods, following the rules of metrology.^{34 35} A recently started coordination action on nanometrology, Co-Nanomet,³⁶ includes a training programme on state-of-the-art characterisation methods for nanomaterials.

An increasing number of reference materials are becoming available, and a database has been set up by the German *Bundesanstalt für Materialforschung*,³⁷ as a support to the activities of ISO/TC 229 and the nanotechnology community at large. One of the leading producers of reference materials is the Commission's JRC, which in 2008 released the IRMM-304 colloidal silicon dioxide reference nanomaterial for use in the analysis of the size of spherical nanoparticles. Other, previously released reference nanomaterials continue to be distributed by the JRC (nanoporous powders and nanoscale thin films on substrates).³⁸ In the absence of formally certified reference materials, it is good practice in collaborative research to use at least a common source of test samples that have been produced according to a well-documented procedure. Such common test materials can develop into reference materials when data about homogeneity and stability become available, and if these are analysed and reported in a transparent manner. For example, the Commission's JRC has organised a repository of representative nanomaterials for testing purposes. It focuses on various forms of titanium dioxide, cerium oxide, zinc oxide, silver, silicon dioxide, and carbon nanotubes, which are targeted by the OECD-WPMN sponsorship programme (see sub-section 6.6.1).

1.3.2. Research on potential human health hazards

Progress has been made in several aspects of research on toxicity testing and on potential effects of nanomaterials on human health. This area has been addressed by numerous completed and ongoing EU-funded projects. The findings from some of these projects were published in the proceedings of the workshop of April 2008, mentioned above.³⁹

In addition to the EU-funded projects, JRC activities in this area focus on the development and harmonisation of methods for the toxicity testing of nanomaterials; and the *in vitro* testing of a representative set of nanomaterials on critical cell lines. They encompass related studies on nanometrology and reference nanomaterials, as well as the development of databases and modelling (applicability of *in silico* methods, and QSARs, quantitative structure-activity relationships).

CANAPE: This integrated project addressed the production of carbon nanotubes on an industrial scale. As part of this work, it considered tests for different endpoints (such as biocompatibility) and their validity in defining the toxicological effects of carbon nanotubes, fullerenes and nanostructured forms of carbon.

NANODERM:⁴⁰ This FP5 project evaluated the quality of skin as a barrier to particles of less than 20 nm in size. The main conclusions were: that titanium dioxide nanoparticles penetrate into the topmost 3-5 corneocyte layers by mechanical action; and that no diffusive transport takes place. Thus penetration studies with static Franz-diffusion cells do not seem adequate for nanoparticles. Clearance is expected to proceed via desquamation. There is deep

³⁴ ISO/IEC Guide 99-12:2007 *International Vocabulary of Metrology - Basic and General Concepts and Associated Terms*, VIM

³⁵ ISO/IEC Guide 43 *Proficiency testing by interlaboratory comparisons*, ISO, Geneva, 1997

³⁶ <http://www.co-nanomet.eu>

³⁷ <http://www.nano-refmat.bam.de/en/>

³⁸ <http://irmm.jrc.ec.europa.eu/catalogue>

³⁹ ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/final_report.pdf

⁴⁰ <http://www.uni-leipzig.de/~nanoderm/>

penetration into hair follicles, but not into vital tissue. Clearance is expected to proceed via sebum excretion.

DIPNA⁴¹ addressed the impact of metallic and ceramic nanoparticles on different types of cells, and designed assays and instruments for field analysis of nanotoxicology.

NanoInteract⁴² developed a platform and toolkit for understanding interactions between nanoparticles and the living world. This included the issue of reproducibility. In 2007, a paper from this project, “Understanding the nanoparticle-protein corona using methods to quantify exchange rates and affinities of proteins for nanoparticles”, received one of six awards of the Proceedings of the (US) National Academy of Sciences (PNAS) for reflecting “the highest standards of scientific excellence and originality”.

CellNanoTox⁴³ developed a multi-disciplinary set of tests and indicators for the toxicological profiling of nanomaterials.

PARTICLE RISK⁴⁴ studied *in vitro* experiments and *in vivo* models for the assessment of adverse health effects in pulmonary, hepatic and cardiovascular target systems. The project developed detailed procedures to investigate the association between short-term variations in air pollution and cardiovascular health, which can be used in future European studies. Data on levels of air pollutants, in particular size and number distributions of particles in urban air, were collected for three European cities.

NANOTRANSPORT⁴⁵ was a support action that studied the behaviour of aerosols released to ambient air from nanomaterials manufacturing, and the efficiency of protective equipment. The main conclusions were as follows: There is considerable evolution of nanoaerosols over time; their average size increases, while their concentration decreases. Natural background aerosols are scavengers for nanoparticles; the time scale for size evolution depends on the concentration of nanoparticles and that of background aerosol. Nanoparticles will be present in size classes other than those in which they were originally emitted. Filtration efficiency for primary nanoparticles less than 80 nm is usually sufficiently high, but their agglomerates may be in the “most penetrating particle size” (MPPS) range of 80 nm to 200 nm.

Impart-Nanotox⁴⁶ was a combination of two coordination support actions that worked on improving the understanding of the impact of nanoparticles on human health and the environment. They made recommendations on regulation and research strategy, and produced a *Guidance Booklet on Safe Handling of Nanoparticles*.

ENRHES⁴⁷ (an FP7 project completed in 2008) was a support action to perform a comprehensive and critical scientific review of the health and environmental safety of fullerenes, carbon nanotubes (CNTs), metal and metal oxide nanomaterials. The review considered sources, pathways of exposure and outcomes of health and environmental concern, informing regulatory activities. A final report is expected soon.

⁴¹ <http://www.dipna.net/>

⁴² <http://www.nanointeract.net/>

⁴³ <http://www.fp6-cellnanotox.net/>

⁴⁴ http://www.iom-world.org/research/particle_risk.php

⁴⁵ <http://research.dnv.com/nanotransport/>

⁴⁶ <http://www.impart-nanotox.org/>

⁴⁷ *Engineered Nanoparticles: Review of Health and Environmental Safety*,
<http://nmi.jrc.ec.europa.eu/project/ENRHES.htm>

Within this area of research, the following FP7 projects started recently, or are expected to start soon:^{48 49}

INTRACELL: Cell analytics at nanoscale; understanding cellular pathways and trafficking, differentiation process, substrate targeting, uptake, efficacy and toxicity; process modelling.

NanoTEST:⁵⁰ Alternative testing strategies for the risk assessment of nanomaterials used in medical diagnostics. This includes high-throughput toxicity-testing protocols, using *in vitro* cell lines (blood, vascular system, liver, lung, central nervous system, digestive system, placenta and kidney) for mechanistic studies (on oxidative stress, inflammation, immunotoxicology, genotoxicity and barrier transport); and validating these with short term *in vivo* studies and by developing *in silico* methods.

ENPRA⁵¹ addresses a part of the hazard assessment of nanomaterials. In particular it aims to identify the critical physicochemical characteristics of nanomaterials, which are responsible for the observed toxicity, by investigating their interactions at the cellular and molecular levels. Such mechanisms are underlying the observed association and developing systems. They will be verified by performing *in vivo* experiments leading to the development of possible high-throughput alternative toxicity tests, using a structure-activity method to facilitate the identification and prediction of possible hazards from nanomaterials. This work will also address the extrapolation of results from *in vitro* to *in vivo* data, and to other relevant occupational or consumer situations, by incorporating all possible data as weight-of-evidence.

Nanommune (with four US partners):⁵² Analysis of immune toxicological effects using *in vitro* and *in vivo* model systems and state-of-the-art *in silico* (transcriptomics) and lipidomics protocols; Comprehensive assessment of hazardous effects of engineered nanomaterials on the immune system.

NeuroNano (with three US, one Brazilian and one Japanese partner):⁵³ Study of the interaction of nanomaterials with fibrillating proteins with *in vitro* and *in vivo* models. Do nanoparticles induce neurodegenerative diseases? Understanding the origin of reactive oxidative species and protein aggregation in the presence of nanoparticles.

NanoReTox (with one US partner): The reactivity and toxicity of engineered nanoparticles: risks to the environment and human health.

InLiveTox: *Intestinal, Liver and Endothelial Nanoparticle Toxicity – Development and evaluation of a novel tool for high-throughput data generation.*

HINAMOX: *Health Impact of Engineered Metal and Metal Oxide Nanoparticles: Response, Bioimaging and Distribution at Cellular and Body Level.*

NANOPOLYTOX: Toxicological impact of nanomaterials derived from processing, weathering and recycling of polymer nanocomposites used in various industrial applications.

⁴⁸ At the time of writing, some of the projects listed in this section were expected to be funded but were still in the negotiation stage. Therefore, the European Commission makes no commitments as to the eventual funding of these projects.

⁴⁹ At the time of writing, not all projects had dedicated websites. Basic information may be found on the CORDIS website, http://cordis.europa.eu/fp7/projects_en.html.

⁵⁰ <http://www.nanotest-fp7.eu/>

⁵¹ *Risk Assessment of Engineered Nanoparticles*, <http://www.enpra.eu/>

⁵² <http://ki.projectcoordinator.net/~NANOMMUNE>

⁵³ <http://www.neuronano.eu/>

Finally, the NANOGENOTOX Joint Action, bringing together eighteen Member States, is funded under the Commission's Second Health Programme.⁵⁴ It focuses on the "safety evaluation of manufactured nanomaterials by characterisation of their potential genotoxic hazard." The nanomaterials considered will include titanium dioxide, silicon dioxide and carbon nanotubes. NANOGENOTOX focuses not only on the generation and exchange of data, but also on the further development of reliable testing methods. It supports the European contribution to the work taking place under the auspices of the OECD-WPNM.

1.3.2.1. Alternatives to Animal Testing

Alternatives to animal testing are relevant to the assessment of both human toxicity and ecotoxicity.

In November 2005 the Commission created the European Partnership on Alternative Approaches to Animal Testing (EPAA). This has promoted cooperation with industry and other stakeholders. The partners are committed to pooling knowledge, research and resources to accelerate the development, validation and acceptance of alternative approaches. The aim is to develop tools in genomics, computational technologies and high-throughput testing systems, to assess the safety of chemicals, including pharmaceuticals, vaccines, food additives, pesticides and cosmetic products, and to achieve an unprecedented decrease in the use of experimental animals.

Extensive research is underway on alternative ways of assessing safety, and on the possibilities of refining, reducing and ultimately replacing animal testing. The most recent commitment was by the Commission, through the FP7 Health programme,⁵⁵ and the European cosmetics industry (Colipa) for research into alternative testing methods. A total Community and private funding of up to EUR 50 million will be allocated in 2010 to research projects laying the scientific foundation for safety testing methods that will be faster and cheaper than animal tests, and have a higher predictive value. The results of the projects may benefit not only the cosmetics industry, but also the pharmaceutical and chemical industries and other relevant sectors.

Before a test method can be used in the context of a product authorisation, regulatory authorities must accept it. The EPAA partners are looking into different possibilities to accelerate that process, through improved information, reapplication of solutions across sectors, and international regulatory dialogue.

The Commission's JRC also hosts the European Centre for Validation of Alternative Methods (ECVAM),⁵⁶ which performs research on the development of alternative testing methods directly targeting animal tests to be replaced. Following scientific validation by ECVAM, the test methods have to be validated in the OECD before their acceptance for global use and a mutual acceptance of data.

In order to promote the development of alternative methods for the regulatory acceptance of nanomaterials and their applications, the EU is funding three projects, NanoTEST, ENPRA and NANOGENOTOX, together with some Member States. NanoTEST and ENPRA will develop alternative testing strategies and high-throughput toxicity-testing protocols, as well as developing *in silico* methods essential for the risk assessment of nanomaterials. This would allow predictions of the hazards of new materials, extrapolating the results from *in vitro* to *in*

⁵⁴ The Second Programme of Community Action in the Field of Health 2008-2013,

http://ec.europa.eu/health/ph_programme/pgm2008_2013_en.htm

⁵⁵ Call FP7-HEALTH-2010-Alternative-Testing

⁵⁶ <http://ecvam.jrc.it/>

vivo, and to other relevant occupational or consumer situations. NANOGENOTOX will develop validated *in vitro* alternatives to animal testing for the genotoxicity of nanomaterials. All three projects will contribute to the harmonisation and formal validation process in the ECVAM and later on in the OECD.

The OECD-WPMN has a steering group (SG7), chaired by Germany and the Commission, on the role of alternative methods for assessing the safety of nanomaterials, which aims at integrating alternative test methods and testing strategies, and supports the validation of methodologies where applicable. Alternative testing methods are an integral part of the sponsorship programme of WPMN.⁵⁷ A report on the subject is expected to be published by the OECD.

1.3.3. Research on potential exposure throughout the life cycle

Research on exposure has so far focused on workplace exposure, as this is potentially the most important exposure route. Two FP6 projects completed in 2009 addressed exposure and measurements: NANOSH⁵⁸ and Nanosafe2.⁵⁹ Nanosafe2 provided information on the effectiveness of a range of risk management measures for occupational exposure. Examples are process enclosure, ventilation and filtering, and personal protective equipment (PPE). The results have been fed into the compilations of guidance documents published by the OECD-WPMN.⁶⁰ NANOSH led to interesting developments in measurement and sampling strategies. The following table summarises the progress made in these projects.

| Item | Project | Description | State of progress |
|---|---------------------|--|---|
| Identification of sources of engineered/ manufactured Nanomaterials and other | NANOSH Nanosafe2 | Combination of measurements to distinguish manufactured nanomaterials from other nanoparticles | Principles demonstration, pilot measurements in labs and industry production sites showing feasibility of their applications |
| Characterisation of particles from sampling, labelling | NANOSH | Use of precipitators for direct deposition of nanomaterials on TEM grid and others (e.g. particle size analysers; scanning microscope) | Pilot studies showed feasibility of its application |
| On-line detection and measurement methods including assessment of various methodologies | Nanosafe2 | Development of new devices for sampling (and on-line detection) including assessment of various methodologies | Demonstration of principles, development of low cost alarm devices, of devices for large size range NPs, of analysers showing feasibility |
| Personal exposure | NANOSH Nanosafe2 | Direct deposition of nanomaterials on TEM grid in breathing zone and other methods | Measurements done in production facilities of nanomaterials and other powders (eg micro zinc oxide) showing feasibility |
| Qualitative assessment of dermal exposure | NANOSH | Introduction of a slightly modified version of a structured questionnaire (DREAM) | Pilot studies showed feasibility of its application and evidence of dermal exposure potential |
| Decrease of particle release during production of nanomaterials | Nanosafe2 | Development of reactor for synthesis of powders | Demonstration of principles showing feasibility, work continues in the project SAPHIR |
| Air purification, respirators, personal protective equipment | NANOSH Nanosafe2 | Filter efficacy testing | Completed and pilot study performed |
| Release of nanomaterials from textiles | Nanosafe2 | Test method and equipment for nanomaterials release | Standard method proposed and proposed for formal standardisation work |
| Calibration | Nanosafe2 | Methods and equipment for measuring instruments calibration | Completed equipment demonstrated at laboratory scale |

⁵⁷ [http://www.olis.oecd.org/olis/2009doc.nsf/LinkTo/NT0000498A/\\$FILE/JT03267857.PDF](http://www.olis.oecd.org/olis/2009doc.nsf/LinkTo/NT0000498A/$FILE/JT03267857.PDF), p. 20

⁵⁸ <http://www.ttl.fi/Internet/partner/Nanosh/>

⁵⁹ <http://www.nanosafe.org/>

⁶⁰ <http://www.oecd.org/dataoecd/36/36/42594202.pdf>

Nanosafe2 worked on devices for measuring workplace exposure, incorporating background subtraction. Furthermore, the EU-funded NanoCap project generated a strategy for occupational hygiene adapted to nanomaterials, involving elements such as the containment process and personal protective equipment.

Within this area of research, the following FP7 projects started recently:

NanoDevice,⁶¹ a large collaborative project, will develop reliable methods and equipment for the measurement of nanoparticles, in particular novel, portable and easy-to-use devices suitable for workplaces.

ENNSATOX: *Engineered Nanoparticle Impact on Aquatic Environments: Structure, Activity and Toxicology*, will in particular examine the long-term environmental and health impacts of a number of commonly used nanoparticles such as zinc oxide and titanium dioxide, used in products such as paints and cosmetics. It will also look at the relationship between the physical structure of the nanoparticles and their toxicity.

NANEX: *Development of Exposure Scenarios for Manufactured Nanomaterials*, is a support action that will collect and review exposure data, exposure metrics, risk management measures and existing models. Its goal is to develop and standardise a catalogue of generic and specific exposure scenarios for nanomaterials, taking their entire life cycle into account, and covering occupational, consumer and environmental exposure. This should help close knowledge gaps in exposure assessment, including risk management.

1.3.4. Research on potential ecotoxicity, environmental fate and behaviour

The NanoInteract project (sub-section 1.3.2) studied the fate and effects of aggregated CeO₂ nanoparticles in water and concluded that no acute toxicity was observed for any of the three different environmental species tested. For chronic aquatic toxicity, it concluded that toxicity is related to the surface area and not exclusively to mass, despite the nanomaterial aggregation. A decrease of feed concentration was also observed in the vicinity of the nanomaterial delivery. A crucial step in making standard ecotoxicity test methods more reliable for nanomaterials is the collection of knowledge on direct and indirect effects of nanomaterials. Hypothesis testing and the assessment of non-standard endpoints may play an important role in this process. Finally, it was concluded that it is advisable to analyse different endpoints and consider the appearance of measurement artefacts and indirect effects.

In order to improve the research in this field by coordinating, and joining forces with, activities in Member States, the SKEP⁶² ERA-NET (Scientific Knowledge for Environmental Protection) was initiated. This is a partnership of 17 national funding agencies in 13 different countries, responsible for funding environmental research. The SKEP network aims to facilitate science-led policy making, and to support evidence-led regulation.

Within this area of research, the following FP7 projects started recently, or are expected to start soon:

NEPHH: *Nanomaterials related Environmental Pollution and Health Hazards throughout their Life Cycle*. The purpose of this project is to identify and rate important forms of nanotechnology-related environmental pollution and health hazards that could result from activities involved in nanostructures throughout their life-cycle, and to suggest means that might reduce or eliminate these impacts.

⁶¹ see, e.g., ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/nanodevice_kai_savolainen.pdf

⁶² <http://www.skep-era.net/site/2.asp>

NanoFATE: *Nanoparticle Fate Assessment and Toxicity in the Environment*. The work seeks to assess the environmental fate and potential risks of specific nanomaterials used in high-volume products, for which recycling is not an option: fuel additives, personal care and antibacterial products. Two commercially relevant nanomaterials derived from each one of three substances (CeO₂, ZnO and Ag), of varying size, surface and core chemistry, will be monitored throughout their post-production life cycles, i.e. from environmental entry as “spent product”, through waste treatment, to their final fates and possible toxic effects.

1.3.5. *Research on life cycle assessment (LCA) of nanomaterials*

Progress has been made in the European Platform on Life Cycle Assessment,⁶³ which developed an International Reference Life Cycle Data System (ILCD) Handbook of technical guidance documents for LCA, to be published in 2009. It is a project of the Commission’s JRC.

In order to allow nanomaterial LCA based on this guidance, it is still necessary to generate relevant data (including toxicology, fate, transport and scaling data). Major efforts are needed to assess fully potential risks and environmental impacts of nanotechnology-based products and nanomaterials (not just those related to LCA). The EU-funded PROSUITE project is further developing LCA into a full analysis of sustainability; this will include some nanomaterials such as those in the OECD-WPMN sponsorship programme (see sub-section 6.6.1).

Within this area of research, the following FP7 projects are expected to start soon, aiming to create a holistic and prospective view on the environmental, health and safety aspects of different nanomaterials:

NanoHouse: *Life Cycle of Nanoparticle-based Products used in House Coating*.

NanoSustain: *Development of sustainable solutions for nanotechnology-based products based on hazard characterisation and LCA*.

1.3.6. *Sources of information on research on health, safety and environmental issues of nanomaterials*

A plethora of research results is appearing in a number of databases, mainly in the form of bibliographic references. It is still necessary to extract data from the published papers to underpin the risk assessment of specific substances in specific applications. European-based and other publicly accessible databases are as follows:

- The EU-funded NHECD⁶⁴ project was launched in December 2008, with the aim of creating a “critical and commented database on the health, safety and environmental impact of nanoparticles” based on data-mining techniques; an overview of all available databases is given on the website of this project.
- EUPHIX,⁶⁵ a web-based knowledge system that presents structured European public health information with a special insight into similarities and differences in various Member States.
- SAFENANO,⁶⁶ a searchable database on reports, journal and magazine articles on health and safety aspects of nanomaterials operated by the Institute of Occupational Health (UK).

⁶³ <http://lct.jrc.ec.europa.eu/eplca>

⁶⁴ <http://www.nhecd-fp7.eu/>

⁶⁵ http://www.euphix.org/object_document/o4581n27010.html

⁶⁶ <http://www.safenano.org/AdvancedSearch.aspx>

- The Nano Archive,⁶⁷ a part of the FP7 project ICPCNanoNet,⁶⁸ provides free access to published nanoscience research in the EU and International Cooperation Partner Countries, related to environmental, health and safety aspects of nanotechnologies,
- The Commission’s JRC developed and launched the NAPIRA hub, an information management system on nanotechnology safety, containing information specific to nanomaterials, as well as information on the methodology used. The intention is to develop this further and adapt it to nanomaterial datasets.
- The OECD-WPMN developed a database⁶⁹ of finalised and ongoing research projects on the risk assessment of nanomaterials (earlier this database was supported by the US Woodrow Wilson Centre).
- Finally, the EU-funded NanoImpactNet⁷⁰ is a coordination action for projects on HSE research, which will also communicate results to stakeholders and their needs back to researchers; and make contributions to infrastructure and training (as mentioned in chapters 2 and 3 below).

1.4. European Technology Platforms

Several European Technology Platforms (ETPs) are either dedicated to nanotechnology applications or address applications in which nanotechnology is highly relevant. Research priorities identified by these ETPs are being taken on board in FP7 calls for proposals. This section outlines the work of the most relevant ETPs. More ETPs than those outlined below are relevant to nanotechnologies, in the sense that the applications pursued in each case can be enabled or enhanced by solutions based on nanotechnology. Examples are EuMaT⁷¹ (Advanced Engineering Materials and Technologies); Hydrogen and Fuel Cell Technology⁷² (in collaboration with the Commission’s JRC); ARTEMIS⁷³ (embedded computing systems); EPoSS⁷⁴ (smart systems integration); and FTC⁷⁵ (future textiles and clothing).

1.4.1. European Nanoelectronics Initiative (ENIAC)

ENIAC (European Nanoelectronics Initiative Advisory Council) is the ETP dealing with nanoelectronics⁷⁶ (see also section 1.2.1). ENIAC develops the Strategic Research Agenda (SRA) for most European research in the field.⁷⁷ It is playing a key role in defining the research topics in nanoelectronics for FP7, as well as for the ENIAC Joint Undertaking (JU). The latter is active since the beginning of 2007, as the legal instrument implementing the more industrially oriented part of the research agenda, along with the CATRENE cluster, while the more upstream research is funded under FP7. The ENIAC ETP is still active as an independent body of the Joint Undertaking, with the general goal of mobilising European efforts in this innovation- and technology-intensive sector.

⁶⁷ <http://www.nanoarchive.org/view/subjects/HA.html>

⁶⁸ <http://www.icpc-nanonet.org/content/view/26/39/>

⁶⁹ http://www.oecd.org/about/0,3347,en_2649_37015404_1_1_1_1_37465,00.html

⁷⁰ <http://www.nanoimpactnet.eu/>

⁷¹ <http://www.eumat.org/>

⁷² http://ec.europa.eu/research/fch/index_en.cfm; this ETP led to the Fuel Cell and Hydrogen JTI

⁷³ <http://www.artemis.eu/>

⁷⁴ <http://www.smart-systems-integration.org/>

⁷⁵ <http://textile-platform.eu/>

⁷⁶ <http://www.eniac.eu/>

⁷⁷ <http://www.eniac.eu/web/downloads/SRA2007.pdf>

The Eureka⁷⁸ cluster CATRENE⁷⁹ for “Application and Technology Research in Europe on Nanoelectronics” is a four-year programme that started in January 2008 and is extendable to eight years. It builds on the success of the previous EUREKA programmes JESSI, MEDEA and MEDEA+ to foster the continued development of a dynamic and competitive European industry in nanoelectronics. The total effort will be around 4,000 person-years per annum, equalling about EUR 6 billion for the extended programme.

1.4.2. *Photonics21 ETP*

Photonics21⁸⁰ unites the majority of the leading photonics industries and relevant R&D stakeholders throughout Europe. At present, there are over 1,400 members from 49 countries. The aim of Photonics21 is to establish Europe as a leader in the development and deployment of photonics in key industrial areas, including ICT, lighting and displays, manufacturing, life science and security. The Strategic Research Agenda for photonics was first published in April 2006.⁸¹ The second SRA will be published in January 2010. Moreover, the market study “Photonics in Europe: Economic Impact” was published in December 2007. This study assessed the size of the European and global market in photonics, identifying those sectors where Europe leads the world.⁸² The Photonics21 Mirror Group, which was set up in July 2007, brings together representatives from the various funding bodies of Member States, to discuss a coordinated strategy for photonics research. This has resulted in an ERA-NET Plus being set up which will jointly fund photonics research.

1.4.3. *Nanomedicine ETP*

The Nanomedicine⁸³ ETP is an industry-led consortium, bringing together the key European stakeholders in the field, including SMEs, hospitals, research organisations and universities. It also includes representatives of funding agencies from Member States and Regions. The Nanomedicine ETP currently has around 130 member organisations, about 40 of which are industrial. It stimulates the collaboration of the stakeholders and provides input on research priorities to the public authorities. The Nanomedicine ETP was founded in September 2005, when it published its long-term strategic vision paper for the sector. It has grown significantly in membership, visibility and impact. The Strategic Research Agenda (SRA) for Nanomedicine was published in November 2006,⁸⁴ with the main aim of putting forward a sound basis for decision-making processes for policy makers and funding agencies, by providing an overview of the needs, challenges, existing technologies and future opportunities in nanomedicine. The SRA also takes into consideration education and training, ethical requirements, risk-benefit assessment, public acceptance, the regulatory framework and intellectual property issues. R&D priorities defined in the SRA are consistently being taken on board. These are outlined in the sub-section on nanomedicine above. Three years after the publication of the SRA for nanomedicine, the updated, industry-driven “Roadmaps in Nanomedicine towards 2020” will be published by the end of 2009, the aim being to identify trends in research and their expected impact on applications, products and markets.

78 <http://www.eureka.be/>

79 <http://www.medeaplus.org/web/about/presentation.php>

80 <http://www.photonics21.org/>

81 http://www.photonics21.org/download/sra_april.pdf

82 http://www.photonics21.org/download/Brosch_Photonics_Europe.pdf

83 <http://www.etp-nanomedince.eu/>

84 <http://www.etp-nanomedicine.eu/public/public/press-documents/publications/strategic-research-agenda>

1.4.4. Sustainable Chemistry (SusChem)

The European Technology Platform for Sustainable Chemistry (SusChem)⁸⁵ seeks to boost research, development and innovation in chemistry, biotechnology and chemical engineering. Chemistry is ubiquitous and vital for the quality of modern life. More and better use of chemistry will enable European society to become more sustainable. This requires major innovations in chemistry, as well as a successful and healthy European chemical industry. Not only is innovation in chemistry a key to the sustainable growth of the European chemical industry, but it also acts as a catalyst for sustainable innovation in upstream and downstream industries, including consumer product sectors. Furthermore, sustainable chemical technologies can improve public confidence in the chemical industry.

The technologies relevant to SusChem include applications in energy (batteries and photovoltaics); health (nanostructured sensors, targeted delivery and HSE); transport (new materials, catalysts and fuel cells); information and communication technologies (new processing technologies, integration of nanostructures, memories and interconnects); and materials. In SusChem's Implementation Action Plan⁸⁶ (IAP) published in December 2006, nanotechnologies are seen as important enabling technologies for the development of new materials for these applications.

SusChem members became involved in more than eighty European research projects addressing transport, energy, health, information and communication technologies, as well as various nanotechnologies directly. SusChem has carried out an impact assessment, which found that the following topics in its IAP have yet to be sufficiently addressed: (i) embedded sensors (e.g. for the safety of wind generators); (ii) energy saving, including efficient lighting; (iii) sealing technologies; (iv) increasing the lifetime and efficiency of batteries, and high-power batteries for transport applications; (v) integration of high-energy batteries for applications in renewable and distributed energy networks; and (vi) supercapacitors using ionic liquid electrolytes for long-life, high-voltage and high-temperature applications.

Taking also into account the current topics of interest in the field of materials technology, it was decided to focus on energy over the next few years, as part of an "Energy Efficiency Cluster". Several other areas are nevertheless also being tackled:

- Energy applications, in particular batteries, (organic) photovoltaics and supercapacitors;
- Health, including nanostructured sensors for biomedical devices and controlled release of bioactive ingredients;
- Transport, including better catalysts for fuel cells, high performance lightweight composites, and nanomaterials for emission abatement;
- Information and communication technologies, including integration of nanostructures into devices; new processing techniques; memories, for instance by the application of nanoscale ferroelectric oxides; interconnects, such as lead-free soldering for power electronics and LEDs; and
- Nanomaterials, including research on new functional materials such as piezoelectric films in microsystems; stabilisation of primary particles on surfaces; nanomaterials for thermoelectrics; corrosion prevention, for instance alternative materials for tinplate passivation;

⁸⁵ <http://www.suschem.org>

⁸⁶ [http://www.suschem.org/content.php?_document\[ID\]=2049&pageId=3217](http://www.suschem.org/content.php?_document[ID]=2049&pageId=3217)

- Finally, self-assembled and smart surfaces are seen as areas of future strategic importance.

The Smart Energy Home Visionary Project of SusChem integrates the possible benefits of using nanomaterials for construction and retrofitting, as smart materials and surfaces, self-cleaning surfaces, sound insulation and for active noise abatement.⁸⁷

The latest SusChem stakeholder event in Prague in February 2009 provided a good overview of the various relevant projects that have been selected for funding under FP7. The event also addressed the benefits and safety of nanomaterials.⁸⁸

1.4.5. *Micro- and Nano-Manufacturing (MINAM)*

The MINAM association,⁸⁹ part of the Manufuture ETP, has continued to grow, with a membership reaching 700 and increasing participation in various policy and implementation activities. The active involvement of European industry, including SMEs, in research has been a key objective of the MINAM association, in addition to its general goal of establishing a new industry for the manufacturing of products based on emerging micro- and nanotechnologies.

MINAM has contributed to the FP7 call planning, in micro- and nano-technology, materials and production, and is actively supporting the development of nanotechnology research with a clear industrial potential. Recommendations from MINAM have recently been supplemented by its roadmapping activities. MINAM is presently involved in work to establish a multi-sectoral, integrating platform, “NANO futures”, with the objectives of linking and representing all ETPs that require nanotechnologies. “NANO futures” should serve as a hub for all relevant sectors:

- Identifying common elements and creating synergies between the ETPs and, where appropriate, with national and regional programmes, ERA-NETs and Networks of Excellence.
- Developing a joint programme of activities with the objective of meeting major challenges; e.g. clean and sustainable manufacturing, competitive and socially responsible commercialisation of nanotechnology, materials, and “horizontal” technologies that will enable competitive and sustainable developments in a range of industrial sectors.

MINAM furthermore contributes to several other activities including the Manufuture ETP and the private-public partnership on “Factory of the Future”. It is worth mentioning in this context the MNT ERA-NET in micro-nano manufacturing.⁹⁰

1.4.6. *European Technology Platform on Industrial Safety (ETPIS)*

ETPIS⁹¹ has coordinated much work on the safety of nanomaterials and related processes, with a dedicated focus group.⁹² The Nanosafety2 project described in sub-section 1.3.3 above is integrated in ETPIS.⁹³

The iNTeg-Risk project, linked to the Focus Group on Emerging Risk of ETPIS, aims to coordinate R&D for improving the management of risks related to new materials and

⁸⁷ http://www.smartenergyhome.eu/downloads/seh_leaflet.pdf

⁸⁸ <http://www.suschem.org/content.php?pageId=3602&lang>

⁸⁹ <http://www.minamwebportal.eu/>

⁹⁰ <http://www.mnt-era.net/MNT/>

⁹¹ <http://www.industrialsafety-tp.org/news.aspx?lan=230&tab=148&nid=88#n88>

⁹² See for example http://euvri.risk-technologies.com/events/event_3/default.htm

⁹³ See for example

<http://www.nanosafe.org/scripts/home/publigen/content/templates/show.asp?P=69&L=EN&SYNC=Y>

technologies. This should reduce the time to market for lead technologies, as well as promoting safety, environmental friendliness and social responsibility as a trademark of advanced EU technologies.

To achieve its goal, iNTeg-Risk relies on five R&D sub-projects of five-year duration. More than 200 tasks focusing on critical factors have been included. The project will essentially: identify specific emerging risks from particular study cases; develop solutions for the identified risks; validate the solutions, disseminate them through the iNTeg-Risk “one-stop shop” and finally ensure continuity.⁹⁴ This project started in December 2008; its initial activities were presented at a conference in June 2009.

1.5. EuroNanoForum 2009

EuroNanoForum 2009 was a four-day conference in Prague on 2-5 June 2009, organised with EU support as an event of the Czech Presidency, under the auspices of the Czech Ministry for Education, Youth and Sports. Previous events in the EuroNanoForum series were organised in 2003, 2005 and 2007 (by the Presidencies of Italy, the United Kingdom and Germany, respectively). The theme of the 2009 conference, which was attended by more than 700 participants from 36 countries, was the sustainable development of European industry and society. It also showcased industrial technologies enabled by nanotechnologies.

The conference highlighted a broad spectrum of nanotechnologies, which could significantly contribute to industries including chemicals, automotive, shipping, aeronautics, construction, textiles, food, biotechnology, healthcare, manufacturing, power generation and storage, electronic and electrical engineering, and environmental remediation. The technology readiness, end-user needs, benefits and risks have been assessed within each of 33 conference sessions. The summaries of these sessions will be used to guide future political actions in research on nanosciences, nanotechnologies and converging sciences.

Following the presentations in plenary sessions and associated panel discussions, the participants arrived at the following conclusions:

1.5.1. Environmentally sustainable and energy-efficient industrial production

The interest in nanomaterials and metal nanoparticles as catalysts is increasing, as a means of achieving reductions in energy consumption and waste streams, as well as improvements in selectivity. Examples include the use of superparamagnetic nanoparticles as heterogeneous catalysts. Other promising concepts to improve energy efficiency are micro reactors and novel reactive media, such as ionic liquids.

Nanotechnology can contribute to significant decreases in energy demand during the construction of new buildings, and in greenhouse emissions from existing ones.

In the transport sector, nanotechnology will have an impact on production and operating costs, and lower the environmental impact for new-generation cars, as well as ships and aircraft.

1.5.2. Energy and environment

Rapidly expanding fields of nanotechnology could contribute to a clean, energy-efficient society and to a plentiful supply of low-cost sustainable and renewable energy, in the form of photovoltaics, wind generation and thermoelectric conversion systems. Any new technologies should be suitable for large-scale application, and capable of providing reliable, stable solutions. Amongst the highlighted research results fulfilling these criteria are solar cells based on dye-sensitised nanocrystalline titanium dioxide.

⁹⁴ <http://www.integrisk.eu-vri.eu/home.aspx?lan=230&tab=51&itm=192&pag=196>

The environmental benefits may in some cases be compromised by unintended consequences of using nanoscale materials, but further data are needed to assess and mitigate possible risks. The climate-forcing effects of natural and engineered nanoparticles in the atmosphere should also be investigated.

1.5.3. *Nanotechnology for sustainable healthcare*

Despite the coordination effort and increased funding for nanomedicine, industrial concerns about the maturity of these technologies still exist. Nevertheless, nanotechnology is helping to bring about important advances in diagnostics, drug delivery and regenerative medicine. Presentations showed how *in vitro* diagnostics are increasingly linked to new drug propositions; *in vivo* imaging is combining different reagents and biomarkers; and biodegradable nanofibre scaffolds are helping to treat previously incurable conditions. The conference called for a better cooperation amongst researchers, clinicians and industry.

1.5.4. *Prospects for industrial nanotechnologies*

Despite the advances in characterisation and analytical tools, some gaps remain. The incremental improvements in silicon-based electronics and improved design of devices are evident, while breakthroughs from bottom-up approaches (e.g. molecular electronics) are still in their infancy. The recommendation is to strengthen public-private partnerships and improve education in Europe.

1.5.5. *Governance of nanotechnology*

- Several interdependent concerns are expressed by industry, including ETPs, and European policy makers, in research and development, health, environment, consumer protection, competitiveness, and so on. There is thus a need for a more effective European cooperation on horizontal nanotechnology issues, in particular standardisation; education; ethical, legal and societal aspects; and communication and outreach.
- Further dialogue and joint actions between governments, funding agencies, industries and research entities are essential in achieving a prosperous sustainable economy in Europe. Only these interactions will overcome the barriers related to infrastructure and knowledge. They are vital in maximising the benefits of cooperative research in nanosciences and nanotechnologies. Also vital is a dialogue with society at large, in order to overcome misconceptions created by ill-informed media comment.
- In order to support the continuing industrialisation of nanotechnology, the development of new products and services should be encouraged. And to respond to broad public demand for safe and responsible research, a larger financial support and wider international cooperation are needed in the fields of safety, health and environmental protection.
- The market success of nanotechnology applications depends very much on the development and validation of measurement and testing methods and the establishment of the corresponding standards.

1.6. International Collaboration in Nanotechnology Research

All themes in the Cooperation part of FP7 are open to the participation of third countries,⁹⁵ where this is justified in terms of the enhanced contribution made in this way to the objectives of FP7. Additionally, participants from international cooperation partner countries (ICPCs) can receive EU funding.

⁹⁵ That is, countries other than Member States and FP7 Associated States

In the NMP Work Programmes in particular, some research topics have been introduced specifically to address international collaboration, for example in the field of environmental, health and safety impacts of engineered nanomaterials. The international participation in nanotechnology projects of NMP was around 5 % in 2007-2008, with 84 participations from 18 third countries.

Further actions to promote international cooperation include:

- Coordinated calls to address objectives of mutual interest (for example with countries having signed S&T cooperation agreements with the EU);
- Specific International Cooperation Actions (SICAs);
- Specific initiatives to promote the participation of ICPCs; these include technical workshops and other events to identify topics of mutual interest for future coordinated calls or SICAs;
- The development of internationally harmonised standards and nomenclature;
- Initiatives to coordinate and exchange research data (such as in environmental, health and safety issues for nanotechnologies);
- Dialogues with major countries on a “code of conduct” for the responsible and safe development of nanotechnology;
- Coordinated actions with researchers in other world regions; and
- The Intelligent Manufacturing Systems (IMS) scheme.⁹⁶

1.6.1. EU-US collaboration on Environmental, Health and Safety Impacts (HSE) of engineered nanoparticles

Two calls have specifically been targeted towards enhancing the EU-US collaboration in the field of HSE impacts of engineered nanoparticles. The first NMP call of FP7 included the topic “Risk assessment of engineered nanoparticles on health and the environment”. Although this topic was not formally within a coordinated call, the call text strongly recommended cooperation with US partners. As a result, three projects were selected for funding with a total of eight US partners (five universities, EPA, NIOSH and the US Geological Survey). The second NMP call of FP7 included the topic “Impact of engineered nanoparticles on health and the environment”, and the call text again recommended cooperation with US and other international teams. Two projects were selected for funding with a total of seven US partners (three universities, EPA, NIOSH, NIEHS and the Woodrow Wilson Centre).⁹⁷ A new coordinated call is included in the 2010 Work Programme of NMP on “Modelling toxicity behaviour of engineered nanoparticles”. On the EU side, an indicative budget of EUR 6 million is dedicated to this call, while on the US side a multi-agency solicitation (EPA, NSF,

⁹⁶ <http://www.ims.org/>

⁹⁷ Although the US participation in proposals submitted in response to these calls has been encouraging, it must be noted that the contract negotiations have often been delayed because of issues related to the legal provisions of the FP7 Grant Agreement. As a rule, the US partners are required to sign the FP7 Grant Agreement even though they do not receive a financial contribution from the Framework Programme. In some cases it has been discovered that because of domestic legislation or the FP7 IPR framework, US participants have been unable or reluctant to sign the Grant Agreement, leading to withdrawals from the project. The situation has improved, but not wholly resolved, after the introduction of new Special Clauses which can be included in the Grant Agreement. Currently negotiations are ongoing on a Coordinated Call, “Option 2”, which would result in “twin projects”. The EC and the US funded projects would be legally separate, but coordinated as tightly as possible. A coordination agreement between the two projects must be concluded to cover issues such as IPR.

NIESH, USDA, NIOSH) is being prepared on “Environmental and biological fate, transport, and transformation of engineered nanomaterials”.

1.6.2. *Collaboration with ICPC countries*

As mentioned above, the number of ICPC participations in nanotechnology projects is fairly good, even though the low selection rates mean that this participation is somewhat scattered. Coordinated calls and Specific International Cooperation Actions (SICAs) can lead to more targeted investment and impact, in addressing areas of mutual interest. The general goal is to boost cooperation with both developed and developing countries. A number of coordinated calls were launched in the last year of FP6 and the first years of FP7, addressing areas of mutual interest to the EU and a number of international partners. Amongst these ICPC partners, one can cite India (on computational material science) and Russia (in the area of sensors). In the context of the coordinated call with India, six projects have been launched with a total EU funding of EUR 5 million.

The 2009 Work Programme of NMP included a coordinated call with Russia on nanotechnology-based sensors, with a total EU funding of EUR 4.65 million and comparable funding from the Russian Federation. Three specific applications were defined, the objective being to fund one project in each:

- Optical chemical sensing with nanoparticles, nano-waveguides and photonic structures;
- Wireless surface acoustic wave physical sensors for operation in a wide temperature range; and
- Sensing of toxic and explosive agents in air based on metal oxide semiconductor nanostructured materials.⁹⁸

A further topic was specified for a support action on the “mapping of nanotechnology and nanostructured materials research infrastructures in Russia”, with EU funding of EUR 350,000.⁹⁹ The projects resulting from the coordinated calls with Russia are expected to start by the end of 2009.

The 2010 Work Programme of NMP includes a coordinated call with Mexico on “adding value to mining at the nanostructure level”. The indicative EC budget for this call is EUR 6 million; some of this is to be dedicated to participants from other ICPCs, from Latin America in particular, in an attempt to promote a regional approach in international cooperation.

⁹⁸ The proposals considered for funding are:

INGENIOUS – developing novel ultra-sensitive and selective nanostructured optochemical sensors for the detection of PAHs (polycyclic aromatic hydrocarbons) and BTX (benzene, toluene, xylene) from complex mixtures. Nanoparticle-based materials with high selectivity and sensitivity will be created for the sensing elements. Application areas will be in industrial process control, occupational health and plants safety.

SAWHOT – involving a new class of material, langasite, and its variant forms in substituting quartz and lithium niobate for research into new wireless SAW sensors operating in an unprecedented temperature range (from -20°C to +650°C).

S3 – developing toxic and explosive gas sensing technologies with higher sensitivity and selectivity at reduced cost, with sensing principles based on molecularly engineered semiconductor nanowires.

⁹⁹ The proposal considered for funding is NANORUCER, which will perform an analysis of strengths and weaknesses of the Russian nanotechnology innovation system, using bibliometrics and patent statistics and a mapping of research activities in Russia on nanotechnology and nanostructured materials. A systematic comparison with the corresponding EU activities should help identify opportunities for future EU-Russia cooperation.

The ICPC participation in EU-funded research is often limited because of insufficient contacts with EU researchers. To ameliorate this situation, the FP7 project ICPC-Nanonet,¹⁰⁰ with partners from the EU, China, India and Russia, aims to provide:

- an electronic archive of nanoscience publications that is freely accessible to researchers around the globe;
- an electronic database of nanoscience organisations and networks in ICPC;
- links to nanoscience researchers and stakeholders across the globe;
- annual reports on nanoscience developments in eight ICPC regions: Africa, Caribbean, Pacific, Asia, Eastern Europe and Central Asia (EECA), Latin America, Mediterranean Partner Countries (MPC), Western Balkan Countries (WBC);
- on-line networking tools (forums and workshops); and
- annual workshops, one in each of EU, China, India, and Russia, which will also be webcast to facilitate greater access.

Networking projects such as ICPC-Nanonet are expected gradually to boost the ICPC participation in EU-funded nanotechnology research.

Special mention should be made of the topic on “Coordination actions with materials researchers in major world regions” in the 2008 Work Programme of NMP. The proposals selected for funding in this topic provide EU researchers with the possibility of networking with major research players in third countries, reinforcing the international dimension of the FP7.

1.6.3. International Dialogue on Responsible Development of Nanotechnology¹⁰¹

The aim of this international dialogue is to promote cooperation with all countries interested in a responsible and sustainable development of nanotechnology. In particular, it provides a forum where the societal impact of nanotechnology can be explored.

The dialogue is of an informal nature and high-level specialists can be invited depending on the agenda of the meetings. It is strictly complementary to other global forums, never duplicating what is done competently and successfully elsewhere, but paving the way for formal discussions in selected areas.

Building on the previous dialogues of 2004 in the US and 2006 in Japan, the European Commission was pleased to organise the 3rd International Dialogue for Responsible Research and Development of Nanotechnology, which was held in Brussels on 11-12 March 2008 and gathered 97 participants representing 49 countries, as well as international organisations, industries and universities.

The Third International Dialogue addressed:

- Nanotechnology governance, debating in more detail (i) the EU-US call for proposals on the impact of nanoparticles on health and the environment, as an example of international research on a topic of global interest; (ii) activities of leading international institutions and organisations; and (iii) the codes of conduct adopted or in preparation. How synergy can be improved between stakeholders was examined, and proposals have been made for the exchange of good practises (e.g. on conditions at the workplace), as well as for coordinated

¹⁰⁰ <http://www.icpc-nanonet.org/>

¹⁰¹ Although the international dialogue is also relevant to other chapters of this report, it is presented here for the sake of completeness.

“observatory” activities, including indicators of responsible and sustainable innovation or the implementation of the codes of conduct.

- “Bridging the gap”, a very informative session illustrating various initiatives, in particular the IBSA initiative (India, Brazil, South Africa), and exploring how to better achieve a meaningful access to knowledge by all countries, in the so-called North-South, North-North or South-South cooperation. Such initiatives deserve further attention in future meetings.
- Debating the progress of the work carried out by the OECD working parties related to nanotechnology, as well as the challenges of metrology, standardisation, definitions and intellectual protection. The importance of launching coordinated activities on global challenges was highlighted, such as nanotechnology for water purification, environmental remediation, and sustainable development in general. Also highlighted were joint projects where the immediate industrial or commercial interest is not apparent, but the societal or environmental benefits are considerable. In addition, organisational challenges were addressed.
- Societal engagement, debating the experience acquired by a global networking of social scientists and hearing the lessons learnt from dialogue with the public in different countries and by different stakeholders. The value of information, communication, dialogue and a constant “listening mode” was consistently highlighted. Good practices were presented and debated.

2. INFRASTRUCTURES

The availability of excellent pan-European Research Infrastructures (RIs) with critical mass and interdisciplinary character is a major challenge for the progress of R&D and industrial innovation in Europe.

ESFRI Roadmap: The European Strategy Forum on Research Infrastructures (ESFRI) was mandated by the Competitiveness Council in 2004 to produce a roadmap for new RIs of pan-European relevance. The ESFRI Roadmap of 2006,¹⁰² with its 2008 update, represents a fundamental effort that addresses the needs of the research community for the next 10-20 years and catalyses a joint vision for new or upgraded RIs.

PRINS¹⁰³ is a pan-European RI for nanostructures, one of the 44 projects identified in the ESFRI Roadmap. It is the infrastructure arm of a broader initiative, the ENIAC ETP (see subsection 1.4.1). It has been conceived as a distributed infrastructure, based on three European centres of excellence, IMEC (Belgium), CEA-LETI (France) and the Fraunhofer Group for Microelectronics (Germany), which will jointly address the new challenges in a coordinated and complementary way and will be put under a common umbrella. PRINS will bring together an unprecedented array of equipment and know-how in topics like high resolution lithography, advanced process steps and modules, electronic systems integration, imaging devices, silicon-based micro-systems, and miniaturised “nano-bio” devices. The open access provided to the scientific community by PRINS will enable innovative research and a truly cross-disciplinary fertilisation of academic and industrial competences. It should allow progress in the scaling of components and circuits (e.g. for nanoelectronics, nanophotonics and nanosystems) by allowing the convergence of “top-down” technology, which is today the

¹⁰² ftp://ftp.cordis.europa.eu/pub/esfri/docs/esfri-roadmap-report-26092006_en.pdf

¹⁰³ <http://www.prins-online.eu>

main enabler of Moore's law, with "bottom-up" methods derived from disciplines such as materials science, chemistry, nanobiotechnology and particle electronics.

PRINS builds on the FP6 projects MNTE and STAR, as well as the FP7 project MNTEE. These projects supported the creation and upgrading of a unique distributed platform for R&D in micro and nanotechnologies. PRINS is now supported financially in its preparatory phase under FP7, with an EC contribution of EUR 1 million. The PRINS PP aims to involve all the stakeholders necessary to make the project move forward; to make decisions on the legal structure, the operation mode and the governance model; and to make financial commitments before construction can start. The cost of the construction phase is currently estimated at EUR 1.4 billion over the period 2009-2015. Member States are the key actors in the emergence of such new RIs, since the EC contribution to the construction costs can only be very limited. Nevertheless, indirect participation in the construction costs is possible, by facilitating loans through the new Risk Sharing Finance Facility (RSFF), an innovative idea of leveraging Community funds available under FP7 through the European Investment Bank (EIB). There is also a possibility of making use of Structural Funds, but to a more limited extent.

EUMINAFab:¹⁰⁴ In addition to supporting the development of new RIs, the Commission supports existing RIs through the Integrating Activity (IA) model (the continuation of the FP6 "I3" model). EUMINAFab is such an integrating activity, on "integrating European research infrastructures for micro-nano fabrication of functional structures and devices out of a knowledge-based multimaterials repertoire". The four-year project started in March 2009 with an EU contribution of EUR 6 million, and involves six academic and four industrial partners. It supports the networking of existing facilities, providing access for over 400 users to a unique portfolio of 36 state-of-the-art installations, and performs joint research activities to improve the services offered to the users. EUMINAFab is expected to develop a knowledge management system for multi-material micro- and nano-processing; stimulate new technical approaches; and accelerate the convergence of miniaturised technologies in response to user requests.

NFFA:¹⁰⁵ The Commission also supports an FP7 Design Study (DS) on "nanoscience foundries and fine analysis". The two-year project started in June 2008 with an EU contribution of EUR 1.8 million, and involves five research institutions. Its purpose is to study the feasibility of a new kind of users' infrastructure for nanoscience, based on "foundry centres" and strongly linked to the large-scale facilities for the fine analysis of matter. The final cluster, forming the basis of the future RI, would consist of three to six centres closely attached to a number of selected European facilities: synchrotron radiation sources; neutron scattering sources; high power lasers, including free electron lasers; high performance computing, and so on. The objective of such a cluster is to enable researchers to access to state-of-the-art synthesis, nanofabrication and analysis tools. NFFA is also designing a repository-type data bank on nanoscience. Last, but not least, NFFA aims at raising the standard of sample definition and characterisation for advanced experiments using leading edge facilities.

Contribution of Networks of Excellence: Beyond the dedicated activities described above, several Networks of Excellence (NoEs) have contributed to infrastructures and training in nanotechnology.

¹⁰⁴ <http://www.euminafab.eu>

¹⁰⁵ <http://nffa.tasc.infm.it>

The experience of the **Nano2Life** NoE is expected to set the basis of a future European nanobiotechnology institute, focused on understanding the nanoscale interface between biological and non-biological entities, and its possible applications, such as eco-efficient and sustainable products; or complex and integrated novel sensor technologies for health care, pharmaceuticals, environment, security and food safety. The appropriateness of a novel infrastructure in nanobiotechnology is being explored through a support action of FP7.

The **Nanoquanta** NoE addressed the quantum mechanics of nanosystems and led to the creation of a virtual infrastructure, the European Theoretical Spectroscopy Facility (**ETSF**).¹⁰⁶ This provides computer codes and expertise for the analysis of the excited states of nanosystems, that is, their electronic and optical properties, thereby supporting further research and industrial applications. ETSF has already attracted many users, including industrial ones. At the end of its funding under FP6 (NMP thematic priority), it was granted funding from the FP7 Capacities programme (e-Infrastructures).

In the area of nanomaterials, several NoEs have led to durable integration. Examples are IDECAT in catalysis, INSIDE-PORES in nano-porous materials, and NANOFUN-POLY in polymer-based nanomaterials.

Efforts of Member States:

As described above, the PRINS project will develop an advanced RI for nanostructures based at IMEC (Belgium), CEA-LETI (France) and Fraunhofer Group for Microelectronics (Germany). Other notable initiatives of Member States are the new International Iberian Nanotechnology Laboratory in Braga; the French initiative to create “nanotechnology integration centres” in Grenoble, Saclay and Toulouse; and the Genesys initiative bringing together European neutron and synchrotron facilities for research in nanotechnology applications.

Through the Genesys initiative,¹⁰⁷ led by the Max Planck Institute, a large consortium of neutron and synchrotron facilities across Europe is working with universities and research centres to bridge the gap between the research needs and future challenges in nanomaterials, and matching these with the latest neutron and X-ray techniques.

With EC support, the VDI Technologiezentrum (VDI-TZ) produced “Nano-map”,¹⁰⁸ showing the regional distribution of relevant national nanotechnology institutions in Germany, grouped by application field and technology. More than 1,200 institutions are shown, including major enterprises, SMEs, networks, research centres, university institutes, associations, and technology transfer and financing institutions.

Coordination actions:

Co-Nanomet is a programme of activities addressing the need within Europe to develop the measurement frame required for successful support to the development and economic exploitation of nanotechnology. Co-Nanomet’s activities focus on the nanometrology needs of European industry and are addressed through four key actions, one of which is the exploitation and development of Infrastructures.

¹⁰⁶ <http://www.etsf.eu/>

¹⁰⁷ Grand European Initiative on Nanoscience and Nanotechnology using Neutron and Synchrotron Sources, <http://genesys.neutron-eu.net/>; Genesys report at

http://www.mf.mpg.de/mpg/websiteMetallforschung/pdf/GENNESYS/GENNESYS_2009.pdf

¹⁰⁸ <http://www.nano-map.de/results/map.php>

Given the high level of investment in nanotechnology capacity-building across Europe, a complementary pan-European view of organisations and associated capabilities in nanometrology is required. The Co-nanomet programme is reviewing current capability, which it will signpost to potential users; and will make recommendations for the development of new nanometrology infrastructures across Europe.

NanoImpactNet¹⁰⁹ is a similar coordination action in the area of risk assessment. It will facilitate collaboration between projects on the health and environmental impacts of nanomaterials; communicate results to stakeholders and their needs back to researchers; create a scientific basis to ensure the safe and responsible development of nanotechnology-based materials and products; and support the development of regulatory measures and implementation of legislation in Europe.

An important future development is the inclusion, in the 2010 call for RI proposals, of a topic to integrate the RIs for the processing, analysis, characterisation and assessment of health and environmental impact of engineered nanomaterials, nanoparticles and nanostructures.¹¹⁰ Like NanoImpactNet, this action is expected to be highly relevant to the research on risk assessment described in section 1.3 above.

3. HUMAN RESOURCES

A new generation of researchers, engineers and skilled workers with a flexible and interdisciplinary approach to R&D is necessary in making rapid progress in nanotechnology. The Commission recognises¹¹¹ the need for the European economy to modernise in order to improve its competitive position. This requires a transition to a knowledge-based economy.

There is a particularly urgent need for training young researchers in Europe in different disciplines, with a focus on nanotechnology. Such an approach should also aim to train open-minded researchers, so that they can work with various disciplines and sectors, and understand the link between fundamental and applied research.

Also necessary is an understanding of market demands and the development of applications. This is another aspect of mobility, which should not only be geographical but also between disciplines and sectors. An effective programme for training and transfer of knowledge should be established. The importance of technological development and the training of highly-qualified technicians should also be considered.

Marie Curie actions:

The general purpose of Marie Curie actions is to improve the career prospects of new researchers, by offering structured training in specific S&T areas, and exposing researchers to other sectors, including the private sector, so that they acquire a broad perspective. Nanotechnology has attracted the interest of researchers, as evidenced by a strong participation in EU-funded and other European activities.

There has been significant support for training in nanotechnology through the Marie Curie actions of FP6, with grants of EUR 161 million, some 8 % of the total budget (even though funds are not earmarked for any particular sector). Training activities in nanotechnology continue to receive funding under the People programme of FP7, with grants of EUR 125 million in 2007 and 2008.

¹⁰⁹ http://www.nanoimpactnet.eu/object_class/nano_men_home.html

¹¹⁰ topic INFRA-2010-1.1.31

¹¹¹ *Towards a European Research Area*, COM(2000)6

Some examples of Marie Curie projects offering training in nanotechnology follow:

– Initial Training Networks (ITN):

NANO-HOST, HERODOT, SOPRANO, FINELUMEN, ELCAT and other projects provide training through research on nanomaterials, such as nanostructured catalytic materials, nanocrystals, nanocomposites, nanostructured metals and metal-oxide interfaces.

MAMINA, MINILUBES and DENDREAMERS offer training in nanotribology and nanomechanics research, nanoscale surface characterisation, nanoporous metallic materials and nanohybrid materials.

FUNMOLS and SEMISPINET offer training in nanodevices. FUNMOLS also provides training in environmental, socio-economic and policy aspects of nanotechnology.

FANTOMAS provides training in nano-opto-magnetism, an emerging field at the interface of coherent non-linear optics, nanophotonics and nanomagnetism.

BIOMINTEC provides training in nanobiotechnology.

HIERARCHY offers a broad training programme in nanosciences and applications.

– Research Training Networks (RTN):

NESPA offers training in nano-engineered superconductors for power applications.

NANOMATCH provides training in nanomaterials, particularly in nanostructured organic-inorganic hybrid systems.

RTNNANO focuses on hybrid nanostructures and nanoelectronics.

NASCENT offers training in nanomaterials for applications in sensors and catalysis.

COMSON offers training in simulation and optimisation in nanoelectronics.

– Early Stage Training (EST):

QIPEST provides training in nanodevices and nanomaterials.

NANOCAGE offers training in a very broad range of techniques used extensively in nanoscale and condensed matter science.

NANOTIME offers training in nanostructured superconductors.

The training programmes of nanotechnology-related Marie Curie projects address two major requirements for future researchers: First, researchers must be able to cope with complex, interdisciplinary problems and analyse them in terms of their chemical, physical and technological aspects. Second, researchers need to combine a wide knowledge of materials, concepts and disciplines in order to find adequate solutions to challenges that are raised in market-driven research. Nanotechnology-related Marie Curie projects provide complex and multidisciplinary research training with contributions from chemistry, physics, biology, materials science, mechanical engineering, opto-electronics, mathematics, modelling and simulation.

Also covered are ethical, socio-economic and policy issues, and public outreach. The diverse applications of nanotechnology can increase people's interest in science and technology. It is therefore an attractive topic for television documentaries, articles in newspapers or popular science magazines, and lectures for non-specialists. Many Marie Curie projects use opportunities to communicate their research results in these ways.

There are close links to the innovation efforts of European companies: Industrial partners directly support the transfer of the results into industrial applications. Collaboration with

industry provides a way of focusing current research efforts, to facilitate the transfer of results to industrial use. The aim is to reduce the existing gap between academically developed technologies and their industrial applications. Commercialisation of academic knowledge is often difficult, but the industrial presence in networks, combined with the expertise of the academic host institutions in setting up spin-off companies, offers opportunities to generate commercial output from the projects.

In Europe, several excellent research teams exist in nanotechnology, but there is a significant fragmentation in the area, because of the existence of separate scientific communities and the absence of thematic identity. Marie Curie projects address the fragmentation in nanotechnology research, creating a coherent framework of research, know-how and training between the various research communities, with the objective of achieving a lasting integration between the main European institutions in the area.

Other Commission activities in education:

The training activities funded by the Commission's lifelong learning programme and the corresponding international activities can support training in nanotechnology. So far, the Erasmus Mundus Programme has supported Masters degrees in three nanotechnology areas¹¹² (although there have been no new projects since 2007). Novel technologies including nanotechnology have been singled out in the Commission's Communication *New Skills for New Jobs*.¹¹³ In June 2008, the European Institute of Innovation and Technology¹¹⁴ (EIT) was set up. The first call for the so-called Knowledge and Innovation Networks¹¹⁵ (KICs), which will constitute the EIC, covers climate change mitigation and adaptation, sustainable energy and the future information and communication society – all being areas of application in which nanotechnology can make important contributions.

Contribution of Networks of Excellence and Integrated Projects: Although all EU-funded research projects may be deemed to include an element of training for new researchers in nanotechnology, one should single out the Networks of Excellence of FP6 (NoEs) and some Integrated Projects, which made valuable contributions in this area.

The **Nano2Life** NoE, which addressed nanobiotechnology, involved 200 scientists, engineers and medical doctors. It contributed to training by bridging the worlds of nanotechnology and biotechnology, by developing a curriculum and tutorials, and by organising summer schools.

The **Nanoquanta** NoE addressed the quantum mechanics of nanosystems and led to the creation of a virtual infrastructure, the European Theoretical Spectroscopy Facility (ETSF). It organised a total of eleven training schools, along with many more scientific conferences and workshops (including the innovative annual Nanoquanta-ETSF Young Researchers' Meeting). More than fifty PhD students were trained collaboratively within the network's own groups.

The **Nanobeams** project created a European PhD School on characterisation techniques using ion and electron beams.¹¹⁶

¹¹² <http://www.emm-nano.org/>
http://www.u-picardie.fr/mundus_MESC/
<http://www.ens-cachan.fr/monabiphot/>

¹¹³ *New Skills for New Jobs - Anticipating and matching labour market and skills needs*, COM(2008)868

¹¹⁴ <http://eit.europa.eu/>

¹¹⁵ <http://eit.europa.eu/kics-call.html>

¹¹⁶ <https://www.nanobeams.org/>

Within the **Nanoker** Integrated Project, three external training programmes will be developed,¹¹⁷ in biomaterials, optics and extreme conditions. Their objectives are: (i) to develop a sense of the underlying complex material response in specific applications and the required multi-functionality of solutions required in biomaterials, optics or extreme conditions; (ii) to provide training in the fields of materials modelling, design, analytical and experimental methods, specific to understanding the behaviour of materials under complex conditions; and (iii) to acquaint scientists and engineers with new processing methods which allow the synthesis of multi-functional nanomaterials. One event specifically addressed workplace and environmental safety.¹¹⁸

The **NanoHand** Integrated Project¹¹⁹ involved most research institutes with experience in the field of micro-robotics and nano-handling, the biggest semiconductor company in Europe, and a number of dynamic nanotechnology SMEs. Its main objective was to deliver the technology needed for the control of nano-objects in an automated, controllable and safe environment. The main outcomes of the project will be demonstrators, including basic hardware, software and the necessary processing strategies. These demonstrators involve robotic production systems inside scanning electron microscopes. Such “nano-robotics” will perform controlled and even automated processing using nanoscale tools, allowing for example carbon nanotubes to be placed as components anywhere in an integrated circuit to replace ordinary components, or to form altogether novel devices that cannot be produced using conventional methods. The short term perspective (CNT-decorated SPM tips) provides technology enabling further advances to be made in AFM (atomic force microscopy). This, in turn, will foster the long term objective of the project, to handle and assemble nanosized objects in the construction of nanoelectronic devices and other uses. Moreover, a Masters course in “nano-manipulation” was developed.

Other training activities:

Two major projects address training in nanoelectronics: To bridge the widening gap between the state of the art of European academia and that of leading industry, the IDESA support action develops training material on the design flow for integrated circuits employing advanced deep sub-micron technologies, and makes it available free of intellectual property rights. The EURO PRACTICE support action is widely recognised as a world-class service offering affordable state-of-the-art CAD tools for educational use and advanced technologies for prototyping. 550 European universities and 50 research centres are using the service.

In the important area of risk assessment, the NanoSMILE¹²⁰ activities within the Nanosafe2 project were designed to provide information and training. These cover potential risks, exposure and dosimetry, and potential impact on health and the environment. The NanoImpactNet coordination action also provides training in this area, with a series of workshops and schools on human and environmental hazards and impact assessment.

Some European Technology Platforms include training in their activities: SusChem, for example, developed an “education database”,¹²¹ because the long-term success of the

¹¹⁷ http://www.nanoker-society.org/index.aspx?id_page=140&ID_Elemento=235

¹¹⁸ http://www.nanoker-society.org/index.aspx?ID_Page=158&ID=365&ID_Plantilla=301&TIPO=asyContenido

¹¹⁹ <http://www.nanohand.eu>

¹²⁰

<http://www.nanosafe.org/scripts/home/publigen/content/templates/show.asp?P=68&L=EN&ITEMID=19>

¹²¹ <http://learning.suschem.org/>

European chemical industry depends on attracting and retaining the best students from school through to higher education. The objectives of this education database are to provide information and courses (from secondary school to PhD level) in the field of sustainable chemistry; assist in the development of new courses; and promote new collaborative activities.

4. INDUSTRIAL INNOVATION

Economic globalisation has changed the world, bringing new opportunities and new challenges. In this new situation, Europe cannot compete unless it becomes more inventive and innovative. Europe's citizens are concerned about important issues ranging from climate change and the depletion of non-renewable resources, to demographic change and emerging security needs, all of which call for collective action to safeguard the European way of life, which combines economic prosperity with solidarity. These legitimate concerns must be turned into an opportunity to enhance Europe's global economic competitiveness. The quicker it can react, the higher the chance of success and the greater prospect that its approach will serve as a global model. From the protection of the environment through eco-innovation to the improvement of individual well-being through more intelligent infrastructure provision, the Commission is convinced that innovation in a broad sense is one of the main answers to people's material concerns about their future.

The European Union has an extraordinary innovation potential. Europe has a long-standing tradition of breakthrough inventions. It has a wealth of creative people and can build on its cultural diversity. It has laid the basis for one of the largest single markets in the world, where innovative products and services can be commercialised on a large scale. It also has a tradition of a strong and responsible public sector, which should be capitalised on.

4.1. General situation

Notwithstanding the large public support for European nanotechnology, private investment in nanotechnology R&D remains low compared to Europe's main competitors (see section 1.1). In fact, the number of new nanotechnology companies created over the last 25 years and still active is significantly lower in Europe than in North America (US and Canada combined). In particular, the number of nanotechnology start-ups is several times higher in North America than in Europe. Moreover, the majority of European nanotechnology companies, mainly located in Germany and the United Kingdom, are much smaller in terms of turnover than their counterparts in the US. With fewer and smaller nanotechnology companies, research efforts in the private sector are bound to be smaller in Europe than in North America.

It is not surprising, therefore, to find that North America is the most active region in the world for registering patents in nanotechnology. In 2003, American applicants registered about 1200 nanotech patents, compared with slightly more than 400 from European applicants. Moreover other countries, such as China, India and the Russian Federation in particular, are emerging in the field of nanotechnology. Although they may still lag behind on most indicators, they are in a position to expand and bridge the gap with Europe. They will probably become serious competitors on the world market and attractive locations for research activities. European industry has yet to build upon the strong and competitive European science base in nanotechnology and to increase its research efforts. The nanotechnology field is undoubtedly a very good example of Europe's difficulty in translating science into innovation, and in creating innovative products and commercial activities from scientific results. This difficulty is revealed by the massive gap in Europe between the development of the science base and that of the nanotechnology industry.

Statistical data, including a general analysis for nanotechnology, can be found in the publications on key figures for the European Research Area (ERA).¹²²

4.2. General innovation policy applicable to nanotechnology

Generating new knowledge and turning it into new products and services is crucial to maintain and enhance Europe's competitiveness. Academia and industry should work closely together and maximise the social and economic benefits of new ideas. Transforming research results into new commercial products is a complex process, involving a broad range of stakeholders. If Europe is to operate as a single market for knowledge, it is not enough simply to increase public investment in research; rather, it is important to create a framework that facilitates knowledge transfer by removing the barriers hindering collaboration between research and industry.

The Commission has a broad innovation strategy.¹²³ The 2006 Communication on innovation, "Putting knowledge into practice: A broad-based innovation strategy for the EU",¹²⁴ points the way forward to accompany industry-led and society-driven innovation with competitiveness and public policies at all levels, as a core element of the renewed Lisbon strategy for growth and jobs. The Communication singles out ten priority actions in a roadmap for action at the national and European levels. These include an improved transfer of knowledge between public research institutions and third parties, including industry and civil society organisations.

The Commission calls upon Member States to make the structural reforms necessary to deliver the results required. In the context of the Lisbon strategy, the Commission has adapted its state aid framework to enable Member States to develop new measures favouring the support of innovation, taking into account the identified shortcomings in this domain. This should also encourage Member States and regions to redirect state support, for instance from structural funds, towards activities that are most directly relevant to the Lisbon agenda.

Other key documents on innovation policy are as follows:

- Commission Recommendation on the management of intellectual property in knowledge transfer activities and Code of Practice for universities and other public research organisations;¹²⁵
- Commission Communication on Improving knowledge transfer between research institutions and industry across Europe: embracing open innovation;¹²⁶
- Voluntary guidelines for universities and other research institutions to improve their links with industry across Europe, accompanying the Communication above;¹²⁷

¹²²

ERA key figures 2007, http://ec.europa.eu/invest-in-research/pdf/download_en/keyfigures_071030_web.pdf;
ERA key figures 2008-2009, http://ec.europa.eu/research/era/pdf/key-figures-report2008-2009_en.pdf;
and more for earlier years at http://ec.europa.eu/invest-in-research/monitoring/statistical01_en.htm

¹²³ http://ec.europa.eu/enterprise/innovation/index_en.htm#2

¹²⁴ COM(2006)502;

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2006:0502:FIN:en:PDF>

¹²⁵ C(2008)1329;

http://ec.europa.eu/invest-in-research/pdf/ip_recommendation_en.pdf

¹²⁶ COM(2007)182;

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2007:0182:FIN:en:PDF>

¹²⁷ SEC(2007)449;

http://ec.europa.eu/invest-in-research/pdf/sec2007449_en.pdf

- Commission Communication on More Research and Innovation - investing for growth and Employment: A Common Approach.¹²⁸

In response to a request from the Council Working Party on Competitiveness and Growth, the Commission services prepared a Progress Report on the broad-based innovation strategy for the EU and the nine strategic priorities for innovation action outlined in the Council conclusions of December 2006.

The Commission's "Competitiveness and Innovation Programme 2007-2013" (CIP),¹²⁹ with a budget of about EUR 3.6 billion, complements FP7 in supporting innovation, with small and medium-sized enterprises (SMEs) as its main target. The programme will support innovation activities (including eco-innovation), provide better access to finance and deliver business support services in the regions. It will encourage a better take-up and use of information and communications technologies and help to develop the information society. It will also promote the increased use of renewable energies and energy efficiency. The CIP is divided into three operational programmes: Entrepreneurship and Innovation Programme (EIP); Information Communication Technologies Policy Support Programme (ICT PSP); and Intelligent Energy Europe (IEE). Nanotechnologies are relevant to all three because of their enabling nature.

When considering Community funding opportunities for research and innovation in nanotechnology, it is important to make the best use of the existing financial instruments, namely FP7, CIP and the Structural Funds of the Cohesion Policy, keeping in mind that they can be combined to fund successive phases of the same project or related projects. For instance, in the period 2007-2013, a total of EUR 86 billion, or 25 % of the Structural Funds,¹³⁰ was allocated to the broad innovation agenda, including support to research, innovative businesses and clusters, entrepreneurship measures, innovative ICT and human resources. These allocations can contribute to the development of nanotechnology, provided that projects meet the priorities of the operational programmes aiming at regional development. For example, just over EUR 21 million was invested in the Centre for Nano Health (CNH) at Swansea University (UK) under the Convergence Objective of the Structural Funds.

An overview of some innovation activities follows:

ProTon Europe,¹³¹ a pan-European network of knowledge transfer offices, was created in 2003 by the Commission and has been self-supporting since 2007. This network consists of over 220 Knowledge Transfer Offices (KTOs) and 10 National Partner Associations. ProTon Europe reaches out to almost 600 universities and public research organisations across Europe. Activities addressing nanotechnology included the 2008 ProTon Europe Annual Conference, which helped form effective partnerships as an essential part of successful knowledge transfer deals.

¹²⁸ COM(2005)488;

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2005:0488:FIN:en:PDF>

¹²⁹ http://ec.europa.eu/cip/index_en.htm;

CIP Work Programme, <http://ec.europa.eu/cip/cipwp.htm>

¹³⁰ http://ec.europa.eu/regional_policy/atlas2007/index_en.htm

¹³¹ <http://www.protoneurope.org>

Technology Innovation International (TII)¹³² is a wide network of innovation and technology transfer specialists, whose members provide support services to firms, with the ultimate aim of developing the knowledge economy and boosting the wealth creation process.

Enterprise Europe Network¹³³ offers support and advice to businesses across Europe and helps them make the most of opportunities in the EU, with emphasis on SMEs.

Europe INNOVA¹³⁴ is a Commission initiative, which aspires to become the laboratory for the development and testing of new tools and instruments in support of innovation, with the view to helping innovative enterprises innovate faster and better. It brings together providers of support on public and private innovation, such as innovation agencies, technology transfer offices, business incubators, financing intermediaries, cluster organisations and others. Within Europe INNOVA, one can mention the Finnish co-operation network for Micro and Nanotechnologies and Adaptive and New Materials.

Pro Inno Europe¹³⁵ is another Commission initiative aiming to become the focal point for innovation policy analysis, learning and development in Europe, promoting learning from the best and contributing to the development of new and better innovation policies in Europe.

4.3. Opportunities in particular technology sectors

This section deals with particular application areas, outlining underlying technologies, their maturity, opportunities and risks.

Recognising the fact that developments in nanomaterials will lead to applications in several different technology sectors, the NanoRoadSME project was funded to develop roadmaps and encourage a knowledge-based approach in SMEs. It produced a report entitled “Overview on Promising Nanomaterials for Industrial Applications”.¹³⁶

Although nanotechnology-related products are already on the market, most areas of nanotechnology are still in the basic research stage. Analyses of potential markets are often vague and inconsistent; nevertheless, market-relevant applications can be expected in the fields of optics, precision engineering, analytics, chemistry, automotive and mechanical engineering, materials management and medical engineering, pharmaceuticals and biology.

The analysis of worldwide research activities has shown that several types of funding are needed: public funding of both basic research and application-driven research; funding for the development of marketable products; and venture capital funds for the establishment of start-ups and spin-offs. It is also recognised that targeted public funding lays a solid foundation for future competitiveness, since it enhances the technological basis and human resources.

An example is the area of ceramics: An analysis of the state of the art shows that realistic market opportunities exist for nanopowders, primarily in those areas where materials with novel property combinations – or at least with remarkably improved tribological, mechanical or corrosion properties – can be produced. Through the use of nanopowders, the current disadvantages of ceramics, which are generally persistent at high temperatures and result in low defect tolerance of ceramic materials and parts – especially the high brittleness – can be minimised. In this, as in other technologies, realising the market potential will only be

¹³² <http://www.tii.org>

¹³³ http://www.enterprise-europe-network.ec.europa.eu/index_en.htm

¹³⁴ <http://www.europe-innova.org/index.jsp>

¹³⁵ <http://www.proinno-europe.eu/index.cfm?fuseaction=page.home>

¹³⁶ http://www.nanoroad.net/download/overview_nanomaterials.pdf

possible if the processes are controllable, the properties are reproducible and the production volumes are sufficiently high to make costs competitive.

Further analyses of market opportunities are needed. The Commission is funding a large support action, ObservatoryNANO,¹³⁷ over four years from 2008 to 2012, with the aim of providing stakeholders with assessments of opportunities and risks within a wide range of application sectors, and enabling them to understand the potential and critical issues. The following technology sectors are covered: (1) Aerospace, Automotive and Transport; (2) Agrifood; (3) Chemistry and Materials; (4) Construction; (5) Energy; (6) Environment; (7) Health, Medicine and Nanobiotechnology; (8) Information and Communication Technologies; (9) Security; and (10) Textiles.

To offer wider access to published nanotechnology research, and opportunities for collaboration between researchers in the EU and International Cooperation Partner Countries (ICPC), the Commission is also funding an open-access electronic archive of publications and patents, ICPC NanoNet.¹³⁸

An outline of industrial possibilities in various sectors follows.

4.3.1. *Nanomaterials for Electronics and Photonics*

The R&D aspects of nanomaterials and nanotechnology in electronics and photonics are described in sub-sections 1.2.1-1.2.2; and 1.4.1-1.4.2.

Nanoelectronics is an enabling technology for all electronic products and services. Logic and memories make up for most of the nanoelectronics market. In addition to its direct economic value, the semiconductor industry is one of the biggest investors in R&D, with typical budgets ranging from 15 % to 20 % of revenue. Regional clusters with a high density of semiconductor industries are also the areas with the highest rate of patenting activity.

Nanoelectronics can be defined as electronics on the deep submicron level – that is, with circuit dimensions of less than 100 nm. The term covers both the manufacturing of ever-smaller semiconductor devices, and advances in molecular electronics exploiting single atoms or molecules. Semiconductor chips with nanoscale features are already in production. The majority of electronic devices now consist of complementary metal oxide semiconductor (CMOS) circuits on silicon wafers, and there is much experience in their low-cost production. Because of its advantageous characteristics and future development potential, experts predict that CMOS will remain the mainstream technology for many years and improvements will continue until at least 2016. Short to medium-term developments will be based on silicon technology.

New nanomaterials – from carbon nanotubes to organic polymers – are being investigated for a wide range of applications, including smaller, flexible displays and more powerful storage devices. Long-term developments of integrated circuits are expected to go beyond the existing silicon CMOS paradigm. This includes alternative schemes to encode information (new logic devices) to enable computing at low power consumption; inventing and developing new information processing technology; and managing heat transfer more efficiently through phonon technology. The current process for integrated circuit fabrication – lithography – may be improved by immersion lithography, computational methods and extreme ultraviolet lithography. There are also a number of wholly new technologies for nanoscale fabrication, including dip-pen lithography and nano imprint lithography. Efforts are made to develop a

¹³⁷ <http://www.observatorynano.eu/project/>

¹³⁸ <http://www.icpc-nanonet.org/>

“universal memory”: one which exceeds the capacity and cost effectiveness of flash memory, whilst maintaining its non-volatility, and improving on the data transfer speed of conventional random access memory. A further impact of nanomaterials is in displays for televisions, portable devices, and other applications; organic LEDs (OLEDs) have already received much attention, but there are also efforts to produce thin-film transistors using carbon nanotubes. Longer term development areas include technologies such as FED and SED, which rely on the field emissive properties of carbon nanotubes.

Moreover, the use of nanoelectronics for the detection of biomolecules has resulted in a range of biochips for routine biomedical diagnosis and the mass screening of patients. A typical use is in transplant surgery, where organs run the risk of being rejected by the patient’s immune system. This risk can be characterised by DNA testing, and the new biochips will allow faster, cheaper and more complete testing of organs and recipients to get a better match in time-critical situations.

Finally, photonic components for applications such as optical networking and photonic-electronic integration are being developed.

4.3.2. *Nanomaterials for the Medical Sector*

The value of the market for pharmaceuticals and medical devices is difficult to assess; estimates range from at least EUR 18 billion, for the European market alone,¹³⁹ to more than EUR 500 billion for the global market.¹⁴⁰ The R&D aspects of nanomedicine are described in sub-sections 1.2.3 and 1.4.3. Although several issues have to be overcome, the use of nanomaterials will have a considerable impact on the medical sector. Impacts are expected in diagnostics including imaging and point-of-care diagnostics; targeted drug delivery; coatings for implants and surgical instruments; drug discovery; and tissue engineering.

Many different nanomaterials are presently used in clinical or pre-clinical trials:

- Nanoparticles with magnetic or supermagnetic properties; titanium dioxide; iron oxide; proteins or peptides; gold; silver; fluorine; manganese; functionalised metal; ligands.
- Nanotubes (used as container for drug delivery).
- Fullerenes (e.g. a modified fullerene is entering clinical trials as an anti-HIV agent).
- Quantum dots (e.g. cadmium selenide core surrounded by a shell of zinc sulphide, for its fluorescence).
- Dendrimers.
- Nanocapsules.
- Nanoparticle suspensions.
- Nanoemulsions.
- Nanocomposites of titanium alloys.
- Nanocoatings of titanium or tantalum.
- Nanoshells.
- Antibodies attached to nanoshells.
- Nanocrystals (e.g. zinc oxide).

¹³⁹ NanoRoadSME project
¹⁴⁰ vision paper of the Nanomedicine ETP

- Nanobiotechnology-based drugs, with a nucleus of iron oxide and an antibody.
- Calcium phosphate (CAP) vaccines.
- Nanoporous materials; nanopores.
- Nanoporous electrode material and nanosized electrodes.
- Nanosized metal colloidal particles.
- Nano-calcium phosphate cements (CPC, nanocement).
- Composites of nanoclays.
- Nanostructured polymer based scaffolds.
- Amphiphilic molecules.
- Supramolecular nanomaterials.
- Nanoscale colloidal particles.

4.3.3. *Nanomaterials for the Energy Sector*

The main challenges to be addressed by applications of nanomaterials in the energy sector are improvements in efficiency, product reliability, safety and lifetime, and the reduction of costs. Three application domains can be identified in this sector: (a) energy conversion and production; (b) energy storage; and (c) energy saving.

The most promising applications in energy conversion are photovoltaics (solar cells), hydrogen conversion (fuel cells), and thermoelectricity (thermoelectric devices). Solar cells will be of interest for local energy supply, if the costs can be significantly reduced and efficient methods for storing electrical energy are available. Cost reduction is expected from dye-sensitised solar cells and organic polymer solar cells. Although nanotechnology may allow a breakthrough, these types of solar cells are still in the research and development phase. The use of fuel cells is currently limited because of high costs. However, improvements brought about by nanotechnology, in membranes, catalysts and electrodes, will lower the cost of low-temperature fuel cells while also improving their efficiency. A potential market is the automotive industry, but suitable fuel cells remain in the R&D phase. Finally, nanostructured materials may be used in thermoelectric devices for recovering waste heat.

For energy storage, the most promising developments relate to rechargeable batteries and supercapacitors. In rechargeable batteries (for example lithium batteries), nanocrystalline materials and nanotubes used as electrode materials have been shown to improve both energy and power density, and also lifetime and charging rates. The miniaturisation of electrodes is a key objective. As in rechargeable batteries, advances in supercapacitors are expected through the use of nanoporous electrode materials. Nanotechnology will open new potential markets for batteries and supercapacitors, or combinations of the two (e.g. in mobile phones and portable computers).

Interesting energy-saving applications are expected in the fields of insulation and efficient lighting. Advances in insulation brought about by nanotechnology will help reduce energy demand and the daily costs in homes and industry. Such advances will be aerogels or smart glazes in the form of ultra thin layers. In the field of more efficient lighting, LEDs and OLEDs¹⁴¹ based on nanotechnology are expected to improve energy efficiency and have a large market impact.

¹⁴¹ Organic light emitting diodes or light emitting polymers (LEPs)

Some examples of nanomaterials used in the energy sector are:

- Nanolayers, such as colloids, organic dye molecules, tungsten trioxide and zinc oxide, for aerogel and smart glass applications;
- Indium gallium nitride for inorganic LEDs;
- Organic nanolayers and nanostructured polymer films for small-molecule LEDs;
- Metal oxide nanomaterials, nanoporous metal oxides or ceramics, and nanocomposite coatings, for nanotube LEDs, fuel additives and catalysts.

4.3.4. *Nanomaterials for the Environment Sector*

Conventional remediation technologies have so far shown only limited effectiveness in reducing the levels of pollutants – especially in soil and water. Nanomaterials will be able to perform significantly better because of their much greater surface area. Various applications have been successfully demonstrated at the laboratory scale, but most of them still require verification of efficacy and safety in the field and are thus still far from market. Further research is also needed to assess the environmental impact of the nanoparticles released. One way of minimising the probability of exposure is to encapsulate the nanomaterial within an inert barrier (e.g. silicon can be used to coat quantum dots) or to immobilise nanostructures onto a surface. Employing such methods can maintain the activity and functionality of the nanomaterial while minimising the probability of nanoparticle dispersion.

4.3.5. *Nanomaterials for the Automotive Sector*

Some new cars already incorporate nanotechnology. From nanotubes in fuel lines, to nanoparticles in scratch-resistant glass coatings or as fuel additives to improve fuel combustion efficiency, nanotechnology has started to enter the transport sector. The sector is benefiting from the development of cost-effective production technologies and better characterisation tools and process control (e.g. PVD and CVD processes for coatings).

For paints and coatings, the properties of traditional powdered ingredients such as fillers and extenders change when their size decreases; and the behaviour of particle surfaces begins to dominate. Such effects include ultraviolet blocking, anti-static and conductive capabilities. Paints and coatings industries were among the first to take advantage of these capabilities three to five years ago. Coatings incorporating nanoparticles are smoother, stronger, and more durable, with only small differences in cost. (More generally, nanomaterials are being widely incorporated in coatings, to obtain results ranging from scratch-resistant and self-cleaning surfaces to moisture-absorbing clothing.)

Nanomaterials presently used for lubrication include nanotechnology-based solid lubricants, which reduce friction between moving parts and minimise wear, save maintenance costs and improve overall engine performance – with resulting reductions in energy consumption and air pollution. An example is the use of new cooling fluids and ferrofluids.

Iron-based nanomaterials injected into certain fluids can be used for suspension and braking systems, as their viscosity can be changed instantaneously to suit conditions.

Nanomaterials presently used for tyres include nanomaterials of inorganic clays and polymers to replace carbon black, leading to tyres that are environmentally friendly and wear resistant; New nanocoatings can reduce weight, improve pressure retention and reduce recycling and incineration costs. In the past few years, European producers of elastomers and inorganic oxides have teamed to produce a green tyre, based on hydrocarbon elastomers reinforced with nanostructured silicon dioxide.

Looking into the future, nanotechnology will keep penetrating into the transport sector, provided that it delivers clear advantages compared to competing solutions, which still offer room for improvements. Coatings and surface treatments are likely to continue to be the fastest growing sectors both in vehicle parts, and in tooling and production equipment. Coating technologies are more mature, can benefit from developments in other sectors and can offer clear benefits in the short term (e.g. increased tooling lifetime).

Eventually, the automotive industry should benefit from nanotechnology developments in energy applications. In principle, almost all automotive components can be improved by nanotechnology. Furthermore, the automotive industry is a major user of sensors and components for new integrated and miniaturised systems. Micro-electro-mechanical systems (MEMS) have been a key driver in many of today's advanced safety systems.

4.3.6. Nanomaterials for the Aeronautics Sector

The main application domains for nanomaterials in the next generation of aerospace vehicles include: airframe and components; coatings and paints; engines and engine components; interior equipment and furnishing.

Nanomaterials presently used include: nanopowders; epoxy matrixes with carbon fibre reinforcements; and ceramics (metallic oxides, nitrides and carbides) for coatings – e.g. zirconium oxide in combination with yttrium oxide is used in coatings and components for gas turbines and jet engines.

No nanomaterials are as yet in industrial use for engines and engine components, although potential applications have been identified for organic matrix composites and ceramic matrix composites in linings, paints, sensors and actuators. These are expected to result in enhancements of mechanical properties. Polymer conductors and ceramics are also likely to permit the modification of certain physical properties, for example to improve fire resistance. New tribological coverings are yet another possibility.

4.3.7. Nanomaterials for the Construction Sector

Buildings within the EU account for 42 % of the total final energy consumption and are responsible for about 35 % of all greenhouse emissions. Therefore, energy-efficient buildings will be crucial for environmentally sustainable development. In this regard, nanotechnology offers several pathways for significant improvements in thermal isolation and reductions in greenhouse emissions.

Increasing the strength and durability of materials is central to the drive to reduce the environmental footprint of buildings, by making more efficient use of resources. This is achieved prior to the construction process, by reducing pollution during the production of materials; and also in service, through an efficient use of energy due to advances in insulation. Two nanomaterials that stand out in their application to construction are silicon dioxide and titanium dioxide. Silicon dioxide is the most common nanomaterial in today's construction industry – in terms of production volume per year. This is being used to strengthen and monitor concrete. The photocatalytic activity of titanium dioxide can be used to break down dirt particles when exposed to sunlight. Self-cleaning windows and roof tiles have already been brought to market. Titanium dioxide may also be used to convert the whole surface of buildings into relatively inefficient but cheap solar cells harvesting energy from sunlight.

Carbon nanotubes (CNTs) may be used to strengthen and monitor concrete. Cost factors and the relatively small number of practical applications are preventing developments, at present. Nevertheless, the construction sector is expected to benefit indirectly from advances in other sectors where CNTs are of interest.

4.3.8. *Nanomaterials for the Textile Sector*

The ETP for the Future of Textiles and Clothing has developed a vision for the very large market in textiles, based on three trends:¹⁴²

- Development of new speciality fibres and fibre composites (and environmentally friendly processes) for innovative textile products, to move from commodities to specialties;
- Development of new textile products for innovative technical applications and “smart” textiles and clothing, to allow new applications;
- Implementation of new design and product development concepts, integrated quality and life cycle management, to offer customisation for clothing and fashion.

Nanotechnology can play a role in all three trends; there are two main possibilities: The first one is an enhancement of present functions and performance of textile materials. For example, fabrics prepared with nanomaterial fillers or using innovative finishing treatments, offer enhanced strength and durability, flame resistance, self cleaning, variable chromatic behaviour, light protection, hydrophilic or hydrophobic properties and antistatic features. These materials can be used for a large variety of applications, including sportswear, protective clothing and packaging. Products with some of these features are already finding their way on the market. The second, longer-term possibility is the development of innovative products, in particular smart or functional textiles with new features and functions – e.g. energy generation; controlled release of drugs or scents; and sensing and actuating capabilities.

4.3.9. *Nanomaterials for the Cosmetics Sector*

Nanomaterials like titanium dioxide and zinc oxide are most widespread, and are highly effective as UV (ultraviolet) filters in sunscreens. Nanotechnology-based materials (so-called bio-composites) in toothpaste promote the natural tooth repair mechanism of saliva. In care products, nanocapsules protect and transport active ingredients and enhance their effect. Fullerenes have begun to be used in cosmetic products for this purpose. Research is underway on improving the physical properties (e.g. the transparency) of finished cosmetic products by using nanomaterials.

Common active ingredients used in cosmetic formulations, such as vitamins or anti-oxidants, can be contained in nanospheres, nanocapsules, oleosomes and liposomes. The production techniques involved, such as coacervation or phase separation, are important, because they can improve the stability of the cosmetic formulation and the active ingredients involved. Some cosmetic products use mineral-based materials and their performance depends on particle size. In sunscreen products, mineral nanoparticles (titanium dioxide and zinc oxide with particle sizes of the order of 20 nm) are efficient UV filters. They transmit, reflect and scatter the visible part of the solar radiation, while absorbing strongly in the UV region.

Fullerenes (C₆₀) are reported to be used in a number of cosmetic products, including face creams. Vesicular systems, including liposomes, have been incorporated in many cosmetic formulations. Liposomes are colloidal particles, typically consisting of phospholipids and cholesterol. The lipid molecules form bi-layers surrounding an aqueous core. Both the bi-layer and the core can be used to entrap and deliver ingredients to the skin. Most studies describe a non-specific targeting effect, whereby vesicles allow accumulation of ingredients in the stratum corneum or other outer layers of the skin. It is unknown to what extent quantum

¹⁴² http://textile-platform.eu/textile-platform/?page_name=Vision

dots, nanotubes or other nanomaterials have found use in marketed cosmetic products, but patents for such products exist.

4.3.10. *Nanomaterials for the Agriculture and Food Sector*

Nanotechnology has the potential, as yet unrealised, to revolutionise the agricultural and food industry, with new tools for the molecular treatment of diseases, rapid disease detection, enhancing the ability of plants to absorb nutrients, and so on. Smart sensors and smart delivery systems will help the agricultural industry combat viruses and other crop pathogens. In the near future, nanostructured catalysts will be available, which will increase the effectiveness of pesticides and herbicides, allowing lower doses to be used. Nanotechnology will also protect the environment indirectly through the use of alternative energy supplies, and filters or catalysts to reduce pollution and clean-up existing pollutants.

Controlled Environment Agriculture (CEA) is a widely used method, which relies on modern technology for crop management. This is an advanced and intensive form of hydroponically-based agriculture. Plants are grown within a controlled environment, so that horticultural practices can be optimised. A computerised system monitors and regulates localised environments, such as fields of crops. CEA technology, as it exists today, provides an excellent platform for the introduction of nanotechnology to agriculture. With many of the monitoring and control systems already in place, nanotechnology-based devices that provide “scouting” capabilities could significantly improve the grower’s ability to determine the best time of harvest for the crop, the vitality of the crop, and food safety issues, such as microbial or chemical contamination. Nanobiotechnology-based sensors will lead to equipment of increased sensitivity, allowing an earlier response to environmental changes. For example, nanosensors using carbon nanotubes or nano-cantilevers are small enough to trap and measure individual proteins; and nanomaterials or nanosurfaces can be engineered to trigger an electrical or chemical signal in the presence of contaminants such as bacteria. Ultimately, precision farming using smart sensors, will lead to an enhanced productivity in agriculture by providing accurate information, thus helping farmers to make better decisions.

Some developments in nanomedicine will also be relevant to animal diseases. Nanotechnology can also be used to clean ground water using, for example nanometre-scale diameter aluminium oxide nanofibres as a water purifier. Filters made from these fibres can remove viruses, bacteria and protozoan cysts from water. Other examples include water purification techniques using specific nanofiltration technologies with holes of 100 nm in size. Some companies are working on water filtration by making use of lanthanum nanoparticles that absorb phosphates from aqueous environments. Applying these effectively, for instance in aquaculture ponds, removes available phosphates and as a result prevents the growth of algae.

The impact of nanotechnology in the food industry has become more apparent over the last few years, with applications including smart packaging to optimise product shelf-life and smart monitoring. Building on the concept of “on-demand” food, the idea of interactive food is to allow consumers to modify food depending on their own nutritional needs or tastes. The concept is that nanocapsules containing flavour or colour enhancers, or added nutritional elements such as vitamins, would remain dormant in the food and only be released when triggered by the consumer. They are also activities related to enhancing the nutritional quality of food through selected additives, and improvements in the way in which the body digests and absorbs food.

4.4. Standardisation and Metrology

4.4.1. Introduction

Standardisation (the process of developing and agreeing upon technical standards) and metrology (the science of measurements and its application) are two separate areas with several overlapping aspects.

Metrology goes beyond standardisation, as it investigates and develops the concepts and approaches that can make measurement results traceable and comparable, not only independent of the time and of the place where the measurement was performed, but also – if possible – independent of the measurement method that was used. Respecting the basic concepts of metrology makes measurement results more reliable and robust. However, in several new or complex measurement fields, such as in nanosciences and nanotechnologies, the properties and the materials that are to be measured are often not sufficiently well understood to be able to disconnect the measurement result from the method that was used to make the measurement – that is, the measurement results are method-dependent. Thus metrology relies on standardisation in the development and improvement of internationally accepted and agreed measurement methods.

Standardisation goes beyond metrology, since it not only deals with measurements, but also with global harmonisation of terminology, products and services. Currently, standardisation for nanotechnology is a much more developed area than that of metrology specific to nanotechnology. This will continue to be the case as long as the measurement needs of industry and innovators, consumers and regulators need to be met without the availability of an improved, in-depth understanding of some of the issues of measurement at the nanoscale.

In terms of research and innovation, the following sub-sections will show what has been achieved so far in both standardisation and metrology for nanotechnology; which initiatives have been launched; and what plans there are for the next few years.

4.4.2. Research, Innovation and Standardisation,

Norms or standards are an important driver of innovation,¹⁴³ as they provide legal certainty for innovative companies, help in creating large-scale markets and in building confidence among consumers. They influence the innovation process through “path dependency”; in other words, when technical specifications are defined, the options for future technological developments are by definition narrowed, since less suitable alternatives are ruled out through a combination of technical and market choices. The Communication on the contribution from standardisation to innovation,¹⁴⁴ adopted in 2008, is a key Commission document on standardisation and innovation.

The Commission services closely monitor follow-up activities outlined here, including the acceleration of standard-setting and the relationship between IPR and standards, since these are of relevance to access to standardisation. Lessons are also learnt from the standardisation projects within the Europe INNOVA initiative (see section 4.2 above). The aim of the Standards Networks¹⁴⁵ in Europe INNOVA is to demonstrate in practice how standards can enhance innovation in Europe. These will also be an issue in some of the new platforms in

¹⁴³ http://ec.europa.eu/enterprise/policies/innovation/policy/standards/index_en.htm

¹⁴⁴ COM(2008)133;

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0133:FIN:en:PDF>

¹⁴⁵ <http://standards.eu-innova.org/>

Phase 2 of Europe INNOVA. In the particular field of standardisation in ICT, a White Paper is being prepared and a workshop¹⁴⁶ has been organised.

The Council Conclusions on standardisation and innovation (25 September 2008) confirmed “the essential contribution which standardisation can make towards developing innovation and competitiveness, by facilitating access to markets, enabling interoperability between new and existing products, services and processes, enhancing protection of users, giving consumers confidence in innovations and disseminating research results”. In order to address this challenge, the CEN and CENELEC Technical Boards agreed in October 2008 on the creation of a joint strategic Working Group to address Standardisation, Innovation and Research, STAIR for short.¹⁴⁷ The STAIR Group had a first meeting on 27 January 2009. CEN-CENELEC STAIR will prepare strategic advice to the two Technical Boards in order to reach an integrated approach between research and innovation and standardisation.

To meet this objective, the STAIR Group will consider the Commission’s policies on innovation and research, and how CEN and CENELEC can contribute as effectively as possible to their implementation. The STAIR Group will address the “standards gap” that was identified by the COPRAS project of FP6. This refers to the fact that, after an EU-funded research project closes, it has no further resources to submit its results to the standards process. The Group will therefore review the funding mechanisms of standardisation in relation to innovation, with a view to identifying solutions to fill the gaps in projects between the R&D and standardisation phases. It will also review the existing CEN-CENELEC documentation on R&D and standardisation and develop new guidance material reflecting the integrated approach. Guidance for researchers to “show the way” to standardisation will be developed. An important challenge for the standards bodies is to make stakeholders aware of the benefits that standardisation can bring to them. National seminars on standardisation and innovation are one means to this end. The STAIR Group will support CEN and CENELEC Members with an interest in such national seminars, by identifying and exchanging “success stories”, where standardisation was instrumental in supporting innovation. In addition to these national seminars, STAIR will also seek to organise a European conference on “standardisation and innovation” targeting research and other relevant organisations. The CEN-CENELEC STAIR has been tasked to address all these challenges (the integrated approach, the production of guidelines, the organisation of seminars and conferences, and so on) in the short to medium term, and should therefore complete its current work plan by the end of 2010.

4.4.3. *Nanotechnology standards: New achievements and developments*

Between 2007 and 2009 the Technical Committees CEN/TC 352 and ISO/TC 229, both initiated in 2005, became fully operational. Several EU national bodies contribute to the ISO work (thirteen EU countries are Participating Members, and three more are Observing Members). Industry associations as well as consumer organisations have become liaison members. The Commission’s Joint Research Centre is very actively involved as a liaison member in both Technical Committees.

To avoid duplication, and because of the global relevance of harmonised standards, EU members have expressed their preference for the development of standards at the ISO level. For topics of mutual interest to both ISO and CEN, work is carried out under the Vienna Agreement, with an ISO or CEN lead. The contribution to the development of ISO standards

¹⁴⁶ http://ec.europa.eu/enterprise/ict/policy/standards/ws08ipr_en.htm

¹⁴⁷ <http://www.cen.eu/cenorm/workarea/advisory+bodies/stair/index.asp>

via CEN is, incidentally, one way of involving in the nanotechnologies standardisation process those EU countries that do not have the means to participate at ISO level.

Forty different ISO documents are currently being developed in ISO/TC 229¹⁴⁸ in the fields of terminology and nomenclature (JWG1); measurement and characterisation (JWG2); health, safety and environmental aspects of nanotechnologies (WG3); and materials specifications (WG4). The following available outputs are noted here:

- ISO/TR 12885:2008: Health and safety practices in occupational settings relevant to nanotechnologies
- ISO/TS 27687:2008: Terminology and definitions for nano-objects – Nanoparticle, nanofibre and nanoplate

The following documents are in the final approval stages and will be available soon:

- ISO 10808: Characterisation of nanoparticles in inhalation exposure chambers for inhalation toxicity testing
- ISO TS 11251: Characterisation of single-wall carbon nanotubes using evolved gas analysis-gas chromatograph mass spectrometry
- ISO TS 10868: Nanotubes – Characterisation of single-wall carbon nanotubes using ultraviolet, visible and near infrared spectroscopy
- ISO TR 80004-1: Terminology – Framework for core concepts
- ISO TS 80004-4: Terminology and definitions for carbon nano-objects
- ISO 29701: Nanotechnologies – Endotoxin test on nanomaterial samples for in vitro systems – Limulus amoebocyte lysate (LAL) test

Finally, the following is a selection of running work items with a particular potential to contribute to closing knowledge gaps in the HSE area:

- ISO 12025: General Framework for Determining Nanoparticle Content in Nanomaterials by Generation of Aerosols
- ISO TR 13329: Preparation of Material Safety Data Sheet (MSDS) for nanomaterials
- ISO TS 14101: Surface characterisation of gold nanoparticles for nanomaterial specific toxicity screening: FT-IR method
- ISO TS 12901-1: Guidance on safe handling and disposal of manufactured nanomaterials
- ISO TR 13014: Guidance on physicochemical characterisation of engineered nanoscale materials for toxicological assessment
- ISO TS 13278: Carbon nanotubes – Determination of metal impurities in carbon nanotubes (CNTs) using inductively coupled plasma-mass spectroscopy (ICP-MS)
- ISO TS 12901-2: Guidelines for occupational risk management applied to engineered nanomaterials based on a control banding approach

Based on criteria of intended document status and relevance for Europe, CEN/TC 352 makes a selection from the large number of ISO/TC 229 work items, and adds these items in its own work programme. The work programme of CEN/TC 352 also includes a number of items led by CEN, but these are currently limited to a “Guide to nanoparticle measurement methods and

¹⁴⁸ http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_tc_browse.htm?commid=381983

their limitations”; a “Guide to methods for nanotribology measurements”; and a “Guide to labelling of manufactured nanoparticles and products containing manufactured nanoparticles”.

It should be noted that ISO/TC 229 and CEN/TC 352 have been initiated in order to fill gaps left by a wide array of other ISO and CEN TCs, which have been dealing with nanotechnology-related standards for many years, in particular, but not only, the measurement and characterisation of particles and materials microstructures. Among the more than thirty current liaison members of ISO/TC 229, are ISO/TC 24 (particle characterisation); ISO/TC 146 (air quality); ISO/TC 201 (surface chemical analysis); ISO/TC 202 (microbeam analysis); ISO/TC 209 (clean rooms and associated environments); ISO/REMCO (ISO Reference Materials Committee); and also the OECD, the IUPAC and the IEC. These TCs and other organisations have an interest in the development of nanotechnology-related standards, and meet twice a year in the Nanotechnologies Liaisons Coordination Group (NLCG), which was initiated after the international workshop of ISO, IEC, NIST and OECD on documentary standards for measurement and characterisation for nanotechnologies (Gaithersburg, Maryland, USA, 26-28 February 2008). The NLCG will “provide a forum to help coordinate and harmonise the work of relevant technical committees and other organisations in the field of nanotechnologies and to identify crosscutting gaps and opportunities and ways to address these.”

Among all ISO standardisation committees, the ISO/TC 24/SC 4 (particle characterisation) today has the largest number of nanotechnology-related standards to offer. The work of this committee is followed by the JRC, which also provides the liaison between ISO/TC 24/SC 4 and ISO/REMCO. The committee’s work programme used to focus on the sizing of particles, but since 2009 it also covers other nanotechnology-relevant properties such as dispersion stability and zeta-potential measurements.

4.4.4. Plans for future standardisation activities: The CEN report to the Commission’s programming mandate and the Commission’s response

In May 2008, the CEN/TC 352 Mandate Report Group submitted a report to the Commission on its Mandate addressed to CEN, CENELEC and ETSI for the development of a programme of standards to take into account the specific properties of nanotechnology and nanomaterials (M/409). This report is based on an extensive review of CEN and CENELEC Technical Committees (TCs), European Technology Platforms (ETPs) and organisations and associations with a possible interest in nanotechnology. It was undertaken in order to determine the level of interest or activity by these groups in current or future standardisation related to nanotechnology. Included in this survey were specific questions about existing and future standards that relate to nanotechnology, which may need to be revised or prepared to take nanotechnology into account.

This work was also linked to the identification of standardisation needs performed within the EU-funded Nanostrand project. Moreover, EU-funded projects in nanotechnology were recently scanned to identify any research activity relevant to standardisation. Relevant projects were grouped in the following clusters:

- Bio applications excluding bio-chips and diagnostics
- Bio-chips, bio-sensors and diagnostics
- Nanomanufacturing and nanomaterials
- Self assembly, templating and nanopatterning
- Tools for nanotechnology

– Toxicology and safety

EU-funded projects in these areas are encouraged to develop and implement active standardisation policies. Other projects, large ones in particular, are including standardisation efforts in their work plans. The picture presented is patchy. A large proportion of the groups consulted either did not respond, or declared little or no current interest or activity. On the other hand, some groups provided very comprehensive replies, indicating their interest or activity, now or in the future. All CEN and CENELEC TCs with responsibility for standards harmonised to New Approach Directives were consulted; and, other than two standards harmonised to the medical devices Directives, there is no positive information that any harmonised standard currently needs review or revision with respect to nanotechnology developments. In view of the many TCs that did not respond, however, it is possible that a complete picture has not been obtained. A lack of certainty or an understanding of the role that standards deliverables can play in supporting the existing and future regulatory framework could have affected the survey results.

The report on the mandate provides a list of proposed standards projects under the three general categories of (i) health, worker and environmental safety; (ii) the Lisbon agenda; and (iii) the societal agenda. The standards deliverables that are likely to be needed are described in this report. These will include primarily CEN Technical Specifications (TSs – normative) and Technical Reports (TRs – informative), although European Norms (ENs – normative and to be implemented by all EU members) will be appropriate in some circumstances. There may also be a role for fast-track deliverables such as Publicly Available Specifications (PASs) and CEN Workshop Agreements (CWAs).

Whichever way the work is developed, there should be close cooperation between CEN/CENELEC and ISO/IEC, and there is scope for Vienna and Dresden Agreements deliverables with both ISO/IEC and CEN/CENELEC leads, in addition to those projects which have already been initiated in collaboration between the nanotechnology TCs of CEN and ISO (CEN/TC 352 and ISO/TC 229). Indeed, the standardisation programme is potentially so large that all available standardisation resources should be embraced. There is likely to be a considerable level of as yet untapped technical expertise in Europe that can be used in the area of standardisation. The level of participation in standards activity in CEN/TC 352 is currently not fully representative of known stakeholders, comprising mostly national standards bodies, national metrology institutes, and a few universities and research establishments. The European standards bodies make the following recommendations:

- (1) A group should be established to focus on the opportunities and needs for nanotechnology standardisation that can arise, for example, within ETPs and EU-funded projects. Membership of such a group should be representative of relevant stakeholders, including TCs and other structures within CEN, CENELEC and ETSI.
- (2) The Commission should require that funded projects consider, where applicable, how their project work can be translated into appropriate standards. The outcome of this consideration should be a project deliverable.
- (3) A programme of standardisation, as described in the report, should be initiated, by means of a standardisation mandate to CEN, CENELEC and ETSI, to encourage the development of nanotechnology-specific standards in Europe, and the participation of European stakeholders in the European standardisation process.
- (4) The Commission should provide clear guidance as to what standards projects are needed to support existing or future legislation.

- (5) Additional incentives should be provided for stakeholders to participate in the nanotechnology standardisation process, for instance through the provision of straightforward means of funding participation in standards committee meetings, in particular those dealing with, and proposing, New Work Items corresponding to the list of required standards listed in this report.
- (6) Because of the current early status of standardisation in nanotechnology, it is recommended that the Commission give a further programming mandate in four to seven years' time. This programming mandate should include funding for expert participants to provide input to the report.

The Commission is currently finalising its response to these recommendations. At the time of writing, it can be concluded that there is an agreement to enhance the links between CEN (e.g. TC 352) and relevant EU-funded projects, to ensure that the pre-and co-normative research work is finding its way into standards and technical specifications.

With regard to the preparation of specific standardisation mandates, a preliminary conclusion is that the activities of CEN (e.g. TC 352) should focus on producing documentary standards in the fields of nomenclature (definitions of nanotechnology-specific terms, materials nomenclature based on nanomaterial structures); characterisation (general guidance on the relevance and limitations of measuring specific properties, new and improved standard measurement methods); exposure (sampling, new and improved standard measurement methods, exposure models and mitigation approaches in the areas of safety related to the workplace, consumer products and environment); and simulation methodologies (simulation of possible workplace, consumer and environment exposure). The simulation of exposure in particular was not explicitly included in the report, but is already part of the ISO/TC 229 work programme; recent research activities and publications led to approaches that should be particularly helpful in assessing various exposures.

Turning to the proposed standardisation work on testing methodologies for toxicology and ecotoxicology, a preliminary conclusion is to leave the pre-normative and co-normative work to the OECD-WPMN, given its current and planned activities in the area (within its sponsorship programme). It is necessary to integrate the standardisation outputs into the OECD-WPMN activities and ensure a good synergy between all relevant efforts. This is considered to be ensured by the Vienna Agreement between CEN and ISO, and the collaboration between CEN/TC 352 and ISO/TC 229, as well as by the links established between ISO/TC 229 and the OECD-WPMN.

4.4.5. Metrology, pre- and co-normative research, and tools for measurement quality assurance

Measurement methods with nanometre-resolution and methods applicable to the assessment of nanoparticles and nanostructured materials are often still under development. The area is research-intensive, because of the many ambiguities in nanomaterials work. In the specific case of nanoparticles, it is, for example, not yet generally realised that particle size distribution is not a fundamental property of the material being studied, but a temporary state of dynamic equilibrium between dispersion and agglomeration in suspensions or aerosols. Such differences between perception and reality present tremendous challenges in nanotechnology. These can only be successfully tackled with the appropriate metrology concepts, and by developing workable reference systems.

As mentioned, there is a need for clarity in the identification of measurands related to several materials properties. There is also a need for new measuring instruments and techniques, which, once developed, will need validation and verification. This is the topic of pre- and co-

normative research, which is performed in industrial research projects (such as FP7) or in collaborative organisations, such as VAMAS (the Versailles project on Advanced Materials and Standards, established in 1982 as one of 18 cooperative projects intended to stimulate trade in new technologies using advanced materials, through pre-standardisation research).¹⁴⁹

In VAMAS, work is undertaken in Technical Working Areas (TWAs), two of which are directly relevant to nanotechnologies – TWA 29, nanomechanics applied to SPM, and TWA 33, polymer nanocomposites. These have now been complemented by the establishment of a new TWA on the characterisation of nanoparticle populations, with projects on airborne nanoparticles, on multiwall carbon nanotubes, and on nanostructured titanium dioxide. VAMAS can provide the outcomes of its pre-normative and co-normative research directly to the ISO standardisation process. To reflect the globalisation of materials research, the VAMAS membership is now wider, with the founding members – Canada, France, Germany, Italy, Japan, UK, USA and the European Commission – joined by Korea, Taiwan, South Africa, Mexico, Australia, Brazil and India between 2007 and 2009.

The relevance of pre- and co-normative research for measurement standards has been emphasised by the adoption of a metrological check-list in ISO/TC 229/JWG 2.¹⁵⁰ This document was developed at the JRC and is beginning to provide more structure to the TC 229/JWG 2 work programme. The development and dissemination of proper metrology concepts in the nanotechnology arena is also the aim of the recently started EU-funded project Co-Nanomet,¹⁵¹ with partners from eight EU countries as well as the JRC. A first Co-Nanomet workshop on the issue of standards for nanotechnologies was included in the EuroNanoForum programme (see section 1.5 above). The Co-Nanomet strategy document for European nanometrology is under development, with a stakeholder workshop planned for 19-20 November 2009, in Braunschweig.

An important metrology activity relevant to nanotechnology also launched in 2008, as the European Association of National Metrology Institutes (EURAMET), has become responsible for the development and execution of the European Metrology Research Programme (EMRP), an Article 169 initiative.¹⁵² Within the current activities of national metrology institutes, much research is being done on nanoscale measurements, which is of direct relevance to standardisation in nanotechnologies. It is important to ensure that work in EURAMET, including EMRP, is properly exploited in future European standardisation work.

With respect to the tools required to advance research and understanding in the nanotechnology field, the issue of suitable reference materials was already mentioned.¹⁵³ The development of reference materials, and their role in the development of new test protocols for the assessment of potential hazards, was a subject in the NanoImpactNet Workshop on standardisation of materials and protocols (Dublin, 20 June 2008). This activity on reference materials is also related to the work of OECD-WPMN (see sub-section 6.6.1), and to the development of the measurement infrastructure required for implementation of regulation.

¹⁴⁹ <http://www.vamas.org/>

¹⁵⁰ ISO/TC 229/JWG2_N095rev1, “Metrological check-list for use in the preparation and evaluation of ISO NWIPs and ISO WDs”

¹⁵¹ <http://www.co-nanomet.eu>

¹⁵² Article 169 of the EC Treaty enables the Community to participate in research programmes undertaken jointly by several Member States, including participation in the structures created for the execution of national programmes.

¹⁵³ Section 1.3 and JRC, <http://irmm.jrc.ec.europa.eu>

4.5. Patents

The following conclusions on nanotechnology patents can be drawn:¹⁵⁴ (i) inventive activities in nanotechnology have been gathering momentum since the late 1990s; (ii) nanotechnology is a set of technologies on the nanometre scale, rather than a single technological field; (iii) higher education and government sectors are important knowledge sources; (iv) science is the driving force of nanotechnology; (v) the number of forward citations to nanotechnology patent applications suggests their high technological and economic values; (vi) recent progress in patent databases opens a way to analyse the nature of nanotechnology; (vii) two kinds of nanotechnologies coexist, “top-down” and “bottom-up”, and it will take some time until bottom-up nanotechnologies have social and economic impacts.

The recently launched FP7 project Nano2Market¹⁵⁵ is expected to provide guidelines for technology transfer in nanotechnology developments. The project will first construct value chains of the transfer of each technology through analysis of specific applications, with regard to development costs, market time, complexity of licensing, and so on. Eventually it will develop and disseminate business models and efficient rules for technology transfer, with special attention to research institutions and SMEs.

4.6. OECD Working Party on Nanotechnology (WPN)

At the international level, innovation is addressed by the OECD Committee on Scientific and Technological Policy (CSTP). Under the CSTP, a Working Party on Nanotechnology (WPN)¹⁵⁶ was established in March 2007 to advise on emerging policy issues of science, technology and innovation related to the responsible development of nanotechnology. This work, together with the activities of the OECD Working Party on Manufactured Nanomaterials (WPMN),¹⁵⁷ is seen as the basic platform to ensure that a balance is being achieved between innovation and capitalising on benefits on the one hand, and a proper risk analysis of nanomaterials on the other hand.

In the period 2007-2008, work on six projects was carried out:

Project A – Indicators and statistics: Reviewing available indicators and statistical information on nanotechnology and drafting a framework for the future collection of such data. There is still a clear lack of internationally comparable and validated indicators and statistics to monitor nanotechnology developments for policy needs.¹⁵⁸ Data on research spending, publications and patents have been collected. These show the significant lag of applications (as shown by patents) emerging from scientific research in the case of nanotechnology; the predominance of the US in patents (even though publications from the EU are comparable in number to those of the US); the current dominance in terms of applications of nanomaterials and nanoelectronics, followed by nanobiotechnology; and the rapid emergence of new players.

¹⁵⁴ More detailed information can be found in the OECD-WPN publication *Capturing nanotechnology's current state of development via analysis of patents*, <http://www.oecd.org/dataoecd/6/9/38780655.pdf>, and the associated presentation, <http://www.oecd.org/dataoecd/25/39/40050927.pdf>
reference not available at the time of writing

¹⁵⁵ http://www.oecd.org/document/36/0,3343,en_2649_34269_38829732_1_1_1_1,00.html
¹⁵⁶ http://www.oecd.org/document/30/0,3343,en_2649_34269_40047134_1_1_1_1,00.html

¹⁵⁷ The OECD Working Party on Manufactured Nanomaterials (WPMN) was established in September 2006, and is looking at international co-operation in health and environmental safety aspects of manufactured nanomaterials.

¹⁵⁸ Report “Nanotechnology: An Overview Based on Indicators and Statistics”

Project B – Companies and the business environment: Complements the statistical work with a set of company case studies across different application areas and countries. It analyses the impacts and business environment of nanotechnology and the challenges for business in developing, adopting and commercialising nanotechnology.¹⁵⁹ The main challenges, apart from research issues, are safety issues (including the public perception of safety); difficulties in production (high processing costs); and a shortage of appropriately qualified human resources.

Project C – International scientific co-operation: This project collected information on research facilities, networks and portals; links to respective websites are given on the WPN website.

Project D – Outreach and public engagement: Promoting the exchange of experience in outreach and public engagement through questionnaires and country case studies. This project surveyed challenges and practices in public engagement, outreach and communication (15 countries and the Commission contributed). Furthermore, a conference and workshop on public engagement were organised in Delft on 30-31 October 2008.

Project E – Policy dialogue: Reviewing national policy approaches to the responsible development of nanotechnology.¹⁶⁰ A questionnaire collected information on nanotechnology policies from OECD Member Countries and the European Commission.

Project F – Global challenges (water): In the first instance, this project focused on the contribution of nanotechnology to the purification of water and the barriers that will need to be addressed,¹⁶¹ since this is a key global challenge, especially for developing countries. It prepared a report entitled “Global Challenges: Water and Nanotechnology”, outlining technologies for purification and management, which include membrane technologies and catalysts. The application of nanotechnology to water is in fact growing more rapidly than the two wider sectors (nanotechnology and water) separately.

A new work programme for the period 2009-2010 has been agreed, building on the work already carried out and aiming to support the development of policy. The six project areas are:

- (1) Statistical framework for nanotechnology;
- (2) Monitoring and benchmarking nanotechnology developments;
- (3) Addressing challenges in the business environment specific to nanotechnology;
- (4) Fostering nanotechnology to address global challenges;
- (5) Fostering international scientific co-operation in nanotechnology; and
- (6) Policy roundtables on key policy issues related to nanotechnology.

In the context of addressing global challenges, a conference on potential environmental benefits was organised jointly with OECD-WPMN (the OECD Working Party on Manufactured Nanomaterials), with Commission and US funding. The “OECD Conference on Potential Environmental Benefits of Nanotechnology: Fostering Safe Innovation-led Growth”, which took place in Paris on 15-17 July 2009,¹⁶² covered both the opportunities and the

¹⁵⁹ Report “Nanotechnology: Impacts on Companies, Business Environments and Policy”

¹⁶⁰ Report “Policy Dialogue – Progress Report and Questionnaire Findings”

¹⁶¹ Report “Global Challenges: Water”

¹⁶² OECD Conference on Potential Environmental Benefits of Nanotechnology: Fostering Safe Innovation-Led Growth, a joint event of OECD-WPN and OECD-WPMN

see http://www.oecd.org/document/40/0,3343,en_2649_37015404_42323688_1_1_1_1,00.html

challenges of the use of nanotechnologies for potential environmental benefit. It is seen as a first milestone in collecting the information and developing the tools, which will help to strike this balance at the international level and avoid eventual trade difficulties. The conference sought to learn from international expertise and identify ways in which policies with the potential to enhance both short-term and long-term economic growth can be pursued. This provided an opportunity for governments, academia and industry to consider the state-of-the-art of nanotechnologies, their potential to bring environmental benefits, and, at the same time, concerns regarding human health and environmental safety. In particular, the conference addressed sustainability and life cycle aspects in a variety of sectors in which nanotechnology has the potential to give rise to environmental benefits. Thus, the conference explored the environmental profiles of emerging nanoscale innovation with the goal of encouraging development of technologies that can result in environmental gain while addressing unintended consequences. The following key areas for case studies were included in this event: energy generation, storage and conservation; catalysis; cleaner production; water treatment and purification; water and soil remediation; novel environmental sensor techniques using nanotechnologies and monitoring devices measuring nanomaterials; and solutions based on sustainable chemistry, including synthesis and processing of chemicals.

A policy roundtable on “International Scientific Co-operation in Nanotechnology” was organised in Braga on 22-23 June 2009, with a further roundtable on “Risk Governance” in Vienna on 25 September 2009. The OECD will publish conclusions from these in due course.

5. SOCIETAL DIMENSION

Societal acceptance is a key aspect of the development of nanotechnologies. The Commission’s role as a policy making body is to take account of people’s expectations and concerns. Not only should nanotechnologies be applied safely and produce results in the shape of useful products and services, but there should also be public consensus on their overall impact. Their expected benefits, as well as potential risks and any required measures, must be fully and accurately presented, and public debate must be encouraged, to help people form an independent view. An effective dialogue with all stakeholders should be in place, so as to steer developments on a path that avoids negative societal impacts. Different actions are undertaken in order to pursue this overall objective.

5.1. Code of Conduct for responsible nanosciences and nanotechnologies research

In February 2008 the Commission adopted a recommendation for a “Code of Conduct for responsible nanosciences and nanotechnologies research”.¹⁶³ The Code promotes responsible research in nanosciences and nanotechnologies, in line with the objectives of the Action Plan. It contains a series of principles and guidelines that Member States, and ultimately all stakeholders in the field of research, are invited to adopt and promote. Council Conclusions on the recommendation were adopted in September 2008.

The Code of Conduct is voluntary and complementary to existing regulations. It does not limit or otherwise affect the right of Member States to grant a wider measure of protection with regard to nanosciences and nanotechnologies research. The Code will be monitored and revised every two years by the Commission in order to take into account worldwide developments in nanotechnology and their integration in European society.

and <http://www.oecd.org/dataoecd/6/1/43284399.pdf>

¹⁶³ Commission Recommendation on a *Code of Conduct for responsible nanosciences and nanotechnologies research*, C(2008)424;

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:116:0046:0052:EN:PDF>

A first international conference on the Recommendation of the European Commission on a code of conduct for responsible nanosciences and nanotechnologies research was held on 7-8 May 2008.

Under the 2009 Work Programme for Science in Society, a call was launched for the coordination of projects which will address the European Commission's recommendation on a code of conduct in Europe and beyond.

In addition to the Commission's Code, other codes have been developed, such as the chemicals industry's "Responsible Care Global Charter 2006";¹⁶⁴ the Responsible Nano Code¹⁶⁵ developed by the Royal Society with other partners; and the Nano Risk Framework,¹⁶⁶ developed by DuPont and the Environmental Defence Fund.

5.2. Ethical issues

The European Union has started the process of developing ethical standards to guide decisions in nanotechnology fields. In doing so, it has taken into account the principle of respect for the rights of individuals, respect for multiculturalism, dialogue and tolerance. These standards inform the ethical evaluation of new technologies and provide the necessary criteria.

5.2.1. Ethical issues in the 7th Framework Programme

Research activities supported by FP7 must respect fundamental ethical principles, including those reflected in the Charter of Fundamental Rights of the European Union. The opinions of the European Group on Ethics in Science and New Technologies are taken into account and this will continue to be the case. Research activities should also take into account the Protocol on the Protection and Welfare of Animals and reduce the use of animals in research and testing, with the ultimate view of replacing it altogether.¹⁶⁷

As was the case in FP6, potential ethical issues are examined for all R&D projects considered under FP7, with ethical reviews carried out where appropriate. These reviews are conducted by dedicated panels of specialist independent evaluators, and are separate from the standard proposal evaluations. A sizeable proportion of nanotechnology proposals considered for funding (from the NMP and Health themes) have been subjected to such ethical reviews. Although the ethical issues raised by such projects were not in fact specific to nanotechnology (they involved animal testing, clinical trials and other tests on humans, and research involving human genetic material), it appears that proposers have in general demonstrated an awareness of the Commission's Code of Conduct for responsible nanotechnology research. Experts involved in ethical reviews have also recognised the applicability of the Code of Conduct.

To support work on ethical, legal and societal aspects of nanomedicine, the Commission funded the *Nanomed Round Table*,¹⁶⁸ a support action that started in 2009, to support decision making in the area of nanomedicine, with regard to ethics, regulation and societal acceptance. Very promising as it is, nanomedicine may add new dimensions to ethical, social and economic issues. It is therefore of primary importance to understand the possible impacts of nanomedicine in advance. It is also important to provide all stakeholders with a well-organised forum to express their needs and requirements, in particular those of patients and society. The recommendations of the project will be based on a thorough analysis of existing documents, a broad debate, and the construction of scenarios on the possible consequences

¹⁶⁴ http://www.cefic.be/Files/Publications/RC_GlobalCharter2006.pdf

¹⁶⁵ <http://www.responsiblenanocode.org/>

¹⁶⁶ <http://nanoriskframework.com/page.cfm?tagID=1095>

¹⁶⁷ (Recital 30) and article 6 of decision on FP7

¹⁶⁸ <http://www.nanomedroundtable.org/>

and impacts of nanomedicine. A further aim is to raise awareness and promote an understanding of the field among policy makers and the wider public, and to propose future structures to consider issues in nanomedicine.

Under the Science in Society Programme (in both FP6 and FP7), several projects on the ethics and governance of nanotechnology have been funded. The first of these will be completed in 2009, leading to conclusions on the ethical and public debate on nanotechnology in Europe. The support actions and research projects under the Science in Society programme mobilise stakeholders and facilitate the building of consensus for prospective research and policy options in this domain.

The FP6 project **DEEPEN**,¹⁶⁹ *Deepening Ethical Engagement and Participation in Emerging Nanotechnologies*, was set up to develop an integrated understanding of the ethical challenges posed by emerging nanotechnologies in real world circumstances, and their implications for civil society, for governance, and for scientific practice.

The FP6 project **NanoCap**,¹⁷⁰ *Nanotechnology Capacity Building NGOs*, was set up to deepen the understanding of environmental and occupational health and safety risks, and ethical aspects of nanotechnology. It organised a structured discussion between environmental NGOs, trade unions, academic researchers and other stakeholders at the European level. In this way, it improved the understanding of nanotechnologies and gave an opportunity to formulate positions within their actual policy contexts, supported by scientific input. As a result, five European NGOs adopted a position on the responsible development of nanotechnology, and the European Trade Union Confederation adopted a resolution representing 60 million workers in Europe.

The FP7 project **NANOPLAT**¹⁷¹ will create a forum on nanotechnology-based consumer products, and evaluate various instruments that have been used on the deliberation of the societal dimension of nanotechnologies across Europe.

The FP7 project **FRAMING NANO**¹⁷² will develop a governance plan covering the requirements for the safe development of nanotechnology, on the basis of a broad international dialogue.

5.2.2. *Promotion of Alternatives to Animal Testing*

A particular requirement in EU policy relates to the promotion of alternatives to animal testing. Several regulatory instruments, such as the Directive on protection of animals used for scientific purposes, and Regulations on REACH and cosmetics, call for the promotion of alternative testing and the refinement, reduction or replacement of animal testing. The cosmetics legislation in particular has prohibited the use of animal testing for cosmetics formulations since 2004; and of acute toxicity tests for ingredients since March 2009. The complete ban on animal testing, also for long-term toxicity studies, will come into force in March 2013. In REACH, the promotion of alternatives to animal testing is one of the main aims of the legislation; its implementation will take place in the new testing proposals and their evaluation in the European Chemicals Agency (ECHA). The Commission has established a partnership with industry, is funding research into alternative testing methods,

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<http://www.geography.dur.ac.uk/Projects/Default.aspx?alias=www.geography.dur.ac.uk/projects/deepen>

170

<http://www.nanocap.eu/Flex/Site/>

171

www.nanoplat.org

172

www.framingnano.eu

hosts the European Centre for Validation of Alternative Methods (ECVAM), and also works on this front in the context of the OECD. Details can be found in sections 1.3, 6.4 and 6.5.

5.2.3. *European Group on Ethics in Science and New Technologies (EGE) and UNESCO*

Following the adoption by the European Group on Ethics in Science and New Technologies (EGE) of an opinion on the ethical aspects of nanomedicine on 17 January 2007,¹⁷³ the EGE may be requested in the future to extend its work to broader nanotechnology issues, on the ethics of nanotechnology for human enhancement, biosecurity and military purposes. The EGE is currently working on an opinion on synthetic biology, which is also relevant.

The Commission also participated in the reflexion of UNESCO's World Commission on Ethics of Scientific Knowledge and Technology (COMEST), which led to recommendations on nanotechnology and ethics.¹⁷⁴

5.3. **Transparency and public engagement**

Transparency and public engagement are key factors in addressing societal concerns regarding the use of nanotechnology, including nanomaterials. The Commission considers that dialogue is indispensable for emerging technologies and that a public acceptance of nanotechnology is crucial for its long-term development. The Commission and a number of the Member States have actively promoted broad dialogues on nanotechnologies, as well as numerous other outreach activities. These events have involved public authorities, scientists, industry associations, consumers, and environmental and other non-governmental organisations. Their coverage complements various other activities by Member States and international organisations. However, surveys¹⁷⁵ have indicated that the European public is still not sufficiently aware of nanotechnology.

The conclusions of the outreach activities detailed later in this section, as well as the activities on ethics and governance described above, show a need for a more permanent public and policy deliberation on nanotechnologies in their broad societal context. The existence of many diverse forums suggests that there is a need for an increased monitoring of public and policy debate at international, European and national levels, for instance by FP7 activities in the years to come.

5.3.1. *Outreach Projects in FP7*

To complement previous outreach projects,¹⁷⁶ the Commission included in FP7 a topic on communication and outreach in nanotechnology, resulting in the funding of four projects which started in 2009, with a combined EU contribution around EUR 5 million.

¹⁷³ The EGE is an independent, multidisciplinary and pluralist advisory group advising the European Commission on how ethical values should be taken into consideration in the preparation and implementation of Community legislation or policies. In finalising its work the EGE received inputs from a number of hearings with experts in the field, decision makers and relevant stakeholders, as well as a public round table that took place in Brussels, in March 2006.

¹⁷⁴ Nanotechnologies and Ethics, Policies and Actions, COMEST Policy Recommendations, UNESCO, 2007, http://portal.unesco.org/shs/en/ev.php-url_id=11371&url_do=do_topic&url_section=201.html

¹⁷⁵ e.g. a Eurobarometer survey, http://www.ec.europa.eu/research/press/2006/pdf/pr1906_eb_64_3_final_report-may2006_en.pdf

¹⁷⁶ Nanologue and NanoDialogue projects of FP6: The Nanologue project developed three possible scenarios of the future development of nanotechnologies in its report "The future of nanotechnology: We need to talk", and developed a "NanoMeter" giving guidance on potential ethical and social issues. The NanoDialogue project organised exhibitions on nanotechnology in eight countries, thereby promoting social information and dialogue in the form of focus groups and public debates

- The NANO-TV project¹⁷⁷ will raise the public awareness of European nanotechnology research, through visual media and the internet. In particular, it will create a series of 14 high-quality free-of-rights Video News Releases (VNRs) for the general public and young people, on the basis of key research results. These will be designed to adapt easily to the needs of a wide range of European TV channels. All VNRs will be made available on the European Research Media Centre website.¹⁷⁸ Key nanotechnology applications will be presented, addressing possible benefits and implications. The videos and associated written material should support a sound, science-based dialogue. Around forty major television networks are expected to broadcast the videos from 2010 onwards.
- The NANOTOUCH project aims to create innovative environments, in which broad audiences can learn about and discuss nanotechnology, by bringing researchers into contact with the public. Three science museums and three science centres will cooperate closely with local universities to create three permanent “Open Nano-lab” centres (in Munich, Milan and Gothenburg) and three “Nano Researcher Live” areas (in Mechelen, Tartu and Naples). Here, the visitors will experience live day-to-day nanotechnology research conducted by young scientists. The process should also offer role models promoting the choice of science as a career.
- The NANOYOU project¹⁷⁹ will carry out a communication and outreach programme in nanotechnology, aimed at the younger European generation. It should involve at least 400 schools, and engage with more than 25,000 students and 4,000 young adults, through programmes in schools, science centres and museums around Europe; and reach a much wider audience through its portal. The programme will combine temporary exhibitions, innovative computer games, experiments and other on-line content. Three main application areas of nanotechnology (nanomedicine, energy and environment, and ICT) will be addressed.
- The TIMEFORNANO project¹⁸⁰ aims to engage the general public, and young people in particular, in discussions on the benefits and potential risks associated with nanotechnology; and to collect opinions and feedback from the participants. The products will use an enquiry-based learning approach, specifically developed in science centres and museums, where people understand by doing. The project will develop a number of informal education products: An interactive nano-kit for student groups; a yearly web contest for youngsters with an artistic approach; and “nano-days”, events and debates for the public at the participating science centres.

Additionally, NanoImpactNet, the European Network on the Health and Environmental Impact of Nanomaterials,¹⁸¹ includes work on an effective two-way communication to ensure efficient dissemination of information to stakeholders and the Commission, while at the same time obtaining input from the stakeholders about their needs and concerns.

¹⁷⁷ <http://www.nano.org.uk/news/feb2009/latest1786.htm>

¹⁷⁸ <http://www.youris.com>

¹⁷⁹ <http://www.nanoyou.eu/>

¹⁸⁰ <http://www.timefornano.eu/timefornanoeu/>

¹⁸¹ http://www.nanoimpactnet.eu/object_class/nano_men_home.html

5.3.2. Commission workshops on communication and outreach

In 2007 the Commission organised two workshops on communication and outreach in nanotechnology, with an intercalated open consultation.¹⁸² The workshops involved experts from the fields of philosophy and sociology of science and science communication; science centres; and artists and graphic designers. In their conclusions,¹⁸³ they identified the following priorities:

- Identifying and surveying target publics to determine their values, concerns and expectations, paying particular attention to “information” (who can reach wider publics).
- Developing new models and tools for communication, dialogue and engagement, addressing both professional and leisure time.
- Stressing the importance of societal choices, with regard to developments.
- Ensuring access to reliable and high-quality information on ethical, social and legal dimensions of nanotechnology and their potential implications for daily life.

5.3.3. Commission information tools

The Commission has published a wide range of information material in many languages and for various age groups, including films. The intention is that at least basic information be available in the EU languages.

Two videos published by the Commission in the past,¹⁸⁴ were complemented in 2009 by a third, *NanoInLife*. This contains a set of supporting stories suitable for media use on key research results in nanotechnology. The video tells the story of a young girl who is discovering the usefulness of nanotechnology-based products in daily life, through interviews with the Nobel Prize winner Harry Kroto and other experts.

Undoubtedly, scientists have a role to play in explaining the principles and applications of nanotechnology to the general public and the press. To support them in public outreach, the Commission has made available the handbook “Communicating Science – a Scientist’s Survival Kit”.¹⁸⁵

Finally, to ensure maximum transparency, the Commission created a specific entry on its Europa website for nanotechnology,¹⁸⁶ containing an overview of all its activities in the field. Frequently asked questions in five languages provide a brief glance at the key issues and activities. There are also links to more specific websites.

5.3.4. Commission dialogues

Although public dialogue and public engagement at the national level are important, the Commission itself maintains an active policy of engagement and consultation. In particular, it invites stakeholders to participate on a continuous basis in the regulatory work, and organised

¹⁸² Workshop on Strategy for Communication Outreach in Nanotechnology, in February 2007; and Workshop on Communication Outreach in Nanotechnology – From Recommendation to Action, on 24-25 October 2007.

¹⁸³ ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/nanooutreach_action_final_mar_08.doc

¹⁸⁴ The first, *Nano: The Next Dimension* (2002), addressed a young public, while the second, *Nanotechnology* (2003), targeted audiences generally interested in science and technology.

¹⁸⁵ http://ec.europa.eu/research/science-society/pdf/communicating-science_en.pdf

¹⁸⁶ ec.europa.eu/nanotechnology

the First and Second Nanotechnology “Safety for Success Dialogues”, in 2007¹⁸⁷ and 2008¹⁸⁸ respectively.

Stakeholders take part as observers in Commission working groups in charge of coordinating the implementation of regulation. Examples include the REACH Competent Authorities Sub-group on Nanotechnologies; the Nanotechnologies Working Group of the Advisory Group on the Food Chain, Animal Health and Plant Health; and the Cosmetics Working Group.

The annual workshops, on the other hand, have shown the need for increased coordination and more exchanges between Member States, regulatory bodies and stakeholders. In addition, the 2008 workshop led to the adoption of ten action points. The “Safety for Success Dialogues”, have become a major platform where stakeholders express their views, both on general issues (such as the regulatory review and risk governance) and on sector-specific questions (for example, food, cosmetics and pharmaceuticals). The third event in the series will take place on 3-4 November 2009.¹⁸⁹

In November 2008, the Commission also organised in Brussels the first “International Risk Assessment Conference”,¹⁹⁰ to launch the “Global Risk Assessment Dialogue”, where issues relevant to nanotechnologies featured prominently.

5.3.5. *Other dialogues and OECD*

The call for dialogue and public engagement in the Action Plan has also been reflected in various other initiatives. The following are only a few examples of the broad range of current debates in Europe.

European industry associations, such as CEFIC, the European Chemical Industry Council,¹⁹¹ and CIAA, the Confederation of Food and Drink Industries of the EU,¹⁹² have set up platforms for dialogue with stakeholders.

European Technology Platforms (ETPs) often have outreach activities and regularly consult with stakeholders.

At national level, various stakeholder dialogues took place (for example in Austria, France, Germany and the United Kingdom). These either focused on particular sectors or were more general in nature; and were either permanent mechanisms (such as in Austria and Germany) or one-off events.

In the context of the EU-US dialogue, representatives of consumer organisations meet with regulators, academia and industry from both sides of the Atlantic, on a transatlantic approach to issues relevant to consumers. In their meeting of 10 June 2009, consumers had a session on “Nanotechnology in Food and Consumer Products”.¹⁹³ A resolution¹⁹⁴ containing consumer requests was presented to the Commission services and US authorities for consideration and follow-up.

The OECD Working Party on Nanotechnology (WPN) organised a “Conference on Outreach and Public Engagement in Nanotechnology”, in Delft on 30 October 2008, as part of its

¹⁸⁷ http://ec.europa.eu/health/ph_risk/ev_20071025_en.htm

¹⁸⁸ http://ec.europa.eu/health/ph_risk/ev_20081002_en.htm

¹⁸⁹ http://ec.europa.eu/health/ph_risk/ev_20091103_en.htm

¹⁹⁰ http://ec.europa.eu/health/ph_risk/documents/ev_20081113_lp_en.pdf

¹⁹¹ <http://www.cefic.be/en/582.html>

¹⁹² http://www.ciaa.be/e-newsletter/nsl2.asp?nsl_id=21&nslidet_id=134

¹⁹³ http://tacd.org/index.php?option=com_docman&task=cat_view&gid=86

¹⁹⁴ http://tacd.org/index.php?option=com_docman&task=cat_view&gid=75

related project. The overall objective was to look at diverse experiences with public engagement and discuss best practice.¹⁹⁵ The WPN is continuing to work in this area, building on the findings so far, with delegate countries undertaking public engagement case studies in 2009 and 2010.

In addition, the OECD Working Parties on Nanotechnology (WPN) and Manufactured Nanomaterials (WPMN) jointly organised the “OECD Conference on Potential Environmental Benefits of Nanotechnology: Fostering Safe Innovation-led Growth”, in Paris on 15-17 July 2009 (see section 4.6). This event showed possible ways of benefiting from nanotechnology, while ensuring human health and environmental safety, showcasing in this way “win-win” opportunities for the environment and the economy.

6. HEALTH, SAFETY, ENVIRONMENTAL AND CONSUMER PROTECTION

While nanotechnology offers the possibility of many beneficial applications, the potential impact of nanomaterials on human health and the environment is not yet fully understood. Nanotechnology products must comply with the high levels of consumer, worker and environmental protection required by the Community.

The EU’s “safe, integrated and responsible” approach to nanotechnologies means that environmental, health and safety aspects must be assessed in parallel to the evolution of nanotechnology applications. This in turn entails substantial additional research funding and the development of dialogues with the involved actors, scientific networks across areas of expertise, and specific training. These should be carried out in cooperation with Member States, international organisations and stakeholders, bearing in mind the fundamental responsibility of manufacturers to ensure the safety of their products. This chapter assesses the actions undertaken and progress achieved, and identifies further necessary actions.

6.1. Nanomaterials on the market

Because of the increasing number of nanomaterials on the market, there is an increasing demand for comprehensive data on their identity, use in various applications, and potential impacts on human health and the environment. In the near future, reporting under various regulatory schemes will constitute an important source of information on nanomaterials and their safety. However, to satisfy current needs, the Commission, industry associations, international organisations and private companies have conducted a number of studies in this regard, which are outlined in this section.

6.1.1. Nanomaterials in research and industrial use

Some nanomaterials have been produced for a long time, for example carbon black and silicon dioxide, while others, such as nano-forms of titanium dioxide and zinc oxide, came to the market in the 1970s. Today, different nano-forms of metal oxides are produced in large quantities.

In 2007 the OECD-WPMN identified fourteen nanomaterials, which were either already on the market or deemed likely to come onto the market at the time, and initiated a sponsorship programme to test these:

- Fullerenes (C₆₀)
- Single-walled carbon nanotubes (SWCNTs)

¹⁹⁵ http://www.oecd.org/document/2/0,3343,en_21571361_41212117_42324482_1_1_1_1,00.html

- Multi-walled carbon nanotubes (MWCNTs)
- Silver nanoparticles
- Iron nanoparticles
- Carbon black
- Titanium dioxide
- Aluminium oxide
- Cerium oxide
- Zinc oxide
- Silicon dioxide
- Polystyrene
- Dendrimers
- Nanoclays

Under the REACH Competent Authorities Sub-group on Nanomaterials (CASG Nano), CEFIC and IMA presented in late 2008 information on the nanomaterials manufactured by their member companies. These are mostly the ones included in the OECD-WPMN list.

In June 2009, the European Cosmetics Association (Colipa) presented¹⁹⁶ a preliminary list of nanomaterials used in currently marketed cosmetics: silicon dioxide, titanium dioxide and zinc oxide are used in the majority of cases; aluminium oxide, carbon black and iron oxides are employed less frequently; and nano-forms of acrylates, cerium oxide, colloidal gold, fullerenes, polyethylene and platinum are used in a few special cases.

The US Environmental Protection Agency (EPA) published in January 2009 an intermediate report from its Stewardship Programme for Nanomaterials.¹⁹⁷ This publication refers to 123 nanomaterials, including various forms of the same substance as separate nanomaterials. Half of the nanomaterials were produced at laboratory scales, and some 50 of them by one company only. The additional nanomaterials, made at volumes comparable to those mentioned above, were lithium titanate, antimony pentoxide, dimethyl siloxide, silanamine, cluster diamonds, manganese oxide, aluminium hydroxide, magnesium oxide, calcium oxide, copper (II) oxide, palladium, platinum, cobalt, rhodium and a quantum dot. It is unknown whether these nanomaterials are on the European market.

Also early in 2009, the European Commission services compiled a preliminary overview of nanomaterials on the market, for the use of the CASG Nano. It concluded that in addition to those listed above, more are being sold on-line for research and industrial purposes. These are aluminium, antimony oxide, barium carbonate, bismuth oxide, boron oxide, calcium oxide, chromium oxide, cobalt oxide, dysprosium oxide, germanium oxide, indium oxide, lanthanum oxide, molybdenum oxide, neodymium oxide, nickel, niobium, palladium, praseodymium oxide, samarium oxide, tantalum, terbium oxide, tungsten, yttrium oxide and zirconium oxide, as well as metals and metal composites. Of these, only dysprosium oxide and samarium oxide have not been pre-registered under REACH as phase-in substances.

On the basis of these evaluations it can be concluded that a variety of nanomaterials are sold on the global market for research or industrial purposes. In cases where these are

¹⁹⁶ http://tacd.org/index2.php?option=com_docman&task=doc_view&gid=249

¹⁹⁷ <http://www.epa.gov/oppt/nano/nmspfr.htm>

manufactured in the EU or imported into the EU, the majority of the substances from which these nanomaterials have been derived seem to have been pre-registered to ECHA as phase-in substances.¹⁹⁸

Various studies indicate¹⁹⁹ that the nanomaterials available in appreciable quantities on the global market fall into the following groups, in order of current market volumes in monetary terms:

- Ceramic nanoparticles including metal oxides (e.g. titanium dioxide, zinc oxide, iron oxide); metal sulphides and nitrides; and other inorganic compounds, all possibly coated with layers of polymers, surfactants, or other inorganic materials.
- Metal nanoparticles, most commonly silver, gold, aluminium and nickel.
- Nanoporous materials (e.g. silicon dioxide, carbon, aluminium oxide, various polymers, metals and silicon).
- Carbon nanotubes (single, multi- or double-walled nanotubes).
- Fullerenes and POSS (made of silicon and oxygen atoms).
- Other carbon nanomaterials (e.g. carbon black, graphite, nanoherring).
- Quantum dots, dendrimers.
- Nanostructured materials (e.g. metal grains and layers of various materials).
- Nanowires, including metallic and semiconducting wires.
- Nanopolymers (e.g. nanostructured polymers and fibres).
- Bionanomaterials (e.g. oligonucleotides, peptides, proteins and bioactive molecules).
- Nanoencapsulations (e.g. liposomes, micelles, solid lipids, polymersomes, emulsions).
- Nanoclays (e.g. layered platelets of clays, generally aluminosilicate ceramic materials).

These materials are used in industrial sectors such as manufacturing, aerospace, automotive, electronics, medicine and pharmaceuticals, oil and gas, in addition to construction, energy and environmental applications (see Annex 2).

Specific applications of ceramic nanomaterials are, for example, in metal and composite coatings for aerodynamic surfaces; and in coated parts to withstand extreme heat and pressure, enhance appearance, prevent deposits, or improve engine efficiency. Titanium dioxide nanomaterials are used, for example, in various coatings (e.g. water, dirt and contamination repellent, self-cleaning, non-stick or UV-resistant coatings). Nanoporous materials are used for insulation (aerogels).

Metal nanoparticles vary greatly in their functions. Silver nanoparticles and other noble metals figure in health care (e.g. as antibacterials for medical instruments and fabrics, and aluminium coatings for prosthetics), while magnetic iron-based alloys are used for energy transmission, and light metals are used in structural applications. Nanostructured alloys and carbon nanotubes render steel much stronger. Specially engineered metal nanoparticles improve properties like flow and dispersion. There are coatings based on polymers and organic-inorganic particles; and filtration solutions using hollow nanofibres or antifouling coatings.

¹⁹⁸ Phase-in substances are, e.g., those previously listed in EINECS

¹⁹⁹ NanoRoadSME and ObservatoryNANO projects; and Lux Research

Carbon nanotubes are used, for example, in polymer composites or foams with high electrical conductivity, in wiring, strengthening of cement, nanostructured devices for active cooling with highly conductive features, embedded in epoxy enabling stronger wind turbine blades, and for sensors. Fullerenes are used, for example, as fillers and in some cosmetics, as well as for resists, anti-static packaging, and nanoimprint lithography.

As regards other carbon nanomaterials, carbon black is used for applications such as car tyres, antistatic textiles, cosmetics and colouring; nanographite for pigment production, as additive to rubber and plastics, and in electrode materials for batteries, fuel cells and supercapacitors; graphitic nanoherring in catalysts; and graphene in electronic applications, such as transparent conductive films, transistors and sensors.

Quantum dots can be used for diagnostics, bio-labels and next-generation solar cells, while quantum dots and dendrimers boost LED output and enable precision optical elements. Nanostructured materials, such as nanostructured metallic alloys and nanoporous materials, are used for stronger and lighter aircraft and automotive parts. They also enhance the performance of rechargeable batteries and catalytic converters. Diamond nanocrystals and nanostructured metal composites enable more durable industrial parts.

Metallic and semiconducting nanowires are used for smaller, faster microchips and memory devices, but also for displays, energy storage devices and sensors. Nanopolymers are used in transport and by packaging industries; and nanofibres for filtration of air or liquids.

Engineered biomolecules (oligonucleotides, peptides, proteins and bioactive molecules) are used for light-control materials and bio-based packaging materials. Liposomes, micelles, solid lipids, polymersomes, emulsions and silicon dioxide shells are used as encapsulators, for example to improve the solubility and bioavailability of ingredients, to protect molecules from degradation, to shield undesirable qualities like taste or smell, to provide optical clarity, or to improve the texture of a cosmetic product.

Nanoclays are layered platelets of clays used primarily as polymer additives, for example in heat-resistant thermoplastics and lightweight and strong moulded automotive parts.

6.1.2. Nanomaterials in consumer products

Although the overall share of consumer products based on nanotechnology is small, consumers may have a direct contact with several types of such products, and may be directly exposed to them in everyday life.

The Woodrow Wilson database collects information on products that are advertised on-line in English and make nanotechnology claims. Such claims are often not substantiated, but rather used for unsupported publicity purposes. The Commission services have also made an assessment of the database and concluded that, of the 755 products covered in January 2009, one third made “nano” claims without any specification of the nanomaterials used. Typical consumer products containing nanomaterials include cosmetics, sunscreens, cleaning products, anti-stain coatings, textiles, paints, and so on. The number of nanomaterials used is relatively small (silver, titanium dioxide, zinc oxide, carbon, silicon dioxide, fullerenes, fullerols, carbon nanotubes, nanomicelles, nanospheres and nanoparticles). The most common claims concern the antimicrobial effects of silver.

In order to get a more robust understanding of the current market situation with regard to the legislative requirements, that is, thresholds for registration under REACH, the Commission services asked a contractor to investigate what nanomaterials are on the EU market today and indicate their potential volumes. A conference to discuss the findings took place on 9 October 2009, and the Commission services will take these results into account in their further work.

6.1.3. Regulatory reporting

REACH²⁰⁰ and **CLP**²⁰¹ will provide knowledge about the safety of nanomaterials, their uses and volumes. Information from the implementation of these Regulations is also the foundation for a number of other legislative areas. Irrespective of the volumes put on the market, CLP provides for the classification and labelling of hazardous substances and their forms (including nanomaterials), and this information is used in legislation. Examples are Directive 98/8/EC²⁰² of the European Parliament and of the Council on the placing on the market of biocidal products; and Council Directive 91/414/EEC²⁰³ concerning the placing of plant protection products.

Under REACH moreover, substances manufactured or imported in volumes of one tonne per year or more have to be registered with the European Chemicals Agency (ECHA). This provides information relevant to the risk assessment and risk management of substances throughout the supply chain.

REACH entered into force on 1 June 2007, and CLP on 20 January 2009. The registration deadlines are determined by the total tonnage²⁰⁴ or toxicity of the substance manufactured or imported. The first registration deadline is 30 November 2010 – for substances at 1,000 tonnes per year or more. This deadline also applies to carcinogens, mutagens and reproductive toxicants (CMRs) with production of one tonne or more per year; and persistent and bioaccumulative toxicants (PBTs) with production of 100 tonnes or more per year. The deadline for the notification to the CLP Inventory of ECHA is generally 3 January 2011. A considerable amount of information stemming from these reportings can therefore be expected in 2011. There are already two examples of registrations of nanomaterials submitted to ECHA – silicon dioxide and carbon black.

Information on the most commonly used nanomaterials will gradually become available after the first set of REACH registrations of high-volume chemicals and the CLP notifications of all hazardous substances by the end of 2010. The former provides a safety dossier for each substance, including different forms and states, while the latter provides available information of hazard classes of substances (including their different forms and states). This will in turn enable the further assessment of their safety and the risk management measures in place. In line with the conditions set out in the regulations, ECHA will assess the information and make the data publicly available via its website.²⁰⁵

Information on what nanomaterials are on the market will also become increasingly available from pre-market intervention schemes under sector-specific regulation. In particular, regulatory change has been made for cosmetic products, meaning that nanomaterials which are not already subject to pre-market authorisation (i.e. preservatives, colorants and UV filters) will be subject to a notification six months before they are placed on the market. If necessary, the Commission will be able to ask the EU Scientific Committee for Consumer Safety (SCCS) for an assessment of the materials.

²⁰⁰ Registration, Evaluation, Authorisation and Restriction of Chemicals (EC Regulation 1907/2006)

²⁰¹ Classification, Labelling and Packaging of substances and mixtures (EC Regulation 1272/2008)

²⁰² O.J. L 123 24.4.1998, P. 1

²⁰³ O.J. L 230 19.8.1991, P. 1

²⁰⁴ Where a nanomaterial is produced together with its “parent” substance, the total tonnage of the substance is used for the determination of its registration timeline and respective information requirements.

²⁰⁵ <http://echa.europa.eu/>

Furthermore, the Regulation on Food Additives²⁰⁶ explicitly stated that a significant change in the production method or in particle size (e.g. preparation in nano-form) of an approved food additive would require a re-evaluation of the substance by the European Food Safety Authority (EFSA) and a new authorisation. No application for an EU authorisation under novel food legislation has been made so far. However, because of the current lack of a legal definition of nanomaterials, there could be some discrepancies with respect to the interpretation and enforcement of the EU food legislation as regards the use of nanomaterials in food. It is expected that the revision of this legislation will bring about the necessary clarity.

6.1.4. *Further work*

The analyses above are all based on publicly available information. There are also uncertainties surrounding what exactly is understood as being a nanomaterial. Such uncertainties notwithstanding, there seems to be a convergent view of what nanomaterials are on the market. Some have been present for a long time. A small proportion of nanomaterials can be found in consumer products. Most nanomaterials currently on the market will probably be registered together with the substances from which they have been derived.

However, the Commission is aware of the need to get a better and more accurate overview of nanomaterials on the market. In line with its policy objectives, and in the light of the debate in the European Parliament on nanomaterials, the Commission intends to present information on the types and uses of nanomaterials, including safety aspects in 2011.

6.2. **Regulation**

6.2.1. *Regulatory Review*

In June 2008, the European Commission adopted the Communication “Regulatory Aspects of Nanomaterials”.²⁰⁷ This regulatory review reflected a commitment expressed in the Action Plan (Action 6d). The Communication was accompanied by a Commission Staff Working Document “providing a summary of legislation in relation to health, safety and environment aspects of nanomaterials, and outlining regulatory research needs and related measures”.²⁰⁸

According to the regulatory review, existing EU legislation covers in principle the potential health, safety and environmental risks in relation to nanomaterials. Certain aspects of production and products are at the same time subject to various Community provisions. The protection of health, safety and the environment needs to be enhanced largely by improving implementation of current legislation. Nevertheless, the Commission acknowledges that regulatory changes may be needed in light of new information becoming available.

The implementation of regulation is facilitated by different types of documents, adopted within the regulatory frameworks, such as implementing legislation, European standards, regulatory and technical guidance documents. These will need to be adapted in order better to cover environmental and health risks in relation to nanomaterials. To do this, however, improved methods are needed for the characterisation of nanomaterials; the assessment of potential hazards, exposure and risks; and risk management measures.

²⁰⁶ (EC Regulation 1333/2008)

²⁰⁷ *Regulatory Aspects of Nanomaterials*, COM(2008)366;

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2008:0366:FIN:en:PDF>

²⁰⁸ SEC(2008)2036;

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=SEC:2008:2036:FIN:EN:PDF>

The Commission and relevant EU Agencies are in the first place reviewing current documents that support implementation, such as implementing legislation, standards and technical guidance, with regard to their applicability to, and appropriateness for, nanomaterials.

Commission working groups in charge of coordinating the implementation of legislation are examining on an ongoing basis whether regulatory change on specific aspects is necessary. In so doing, they are taking into account the continuously generated information addressing the identified knowledge gaps, and relevant work that has been carried out at national and international level.

In an opinion adopted on 24 April 2009,²⁰⁹ the European Parliament questions whether, in the absence of any provisions in Community law specific to nanotechnology, legislation can be deemed adequate to cover the risks related to nanomaterials. Given the lack of appropriate data and assessment methods, the Parliament considers that regulatory change is necessary to address risks in relation to nanomaterials in an appropriate way. The Parliament therefore asks the Commission to review all relevant legislation within the next two years, to ensure safety over the whole life cycle of nanomaterials in products. The Parliament considers it particularly important to address nanomaterials explicitly, at least within the scope of legislation on chemicals, food, waste, air and water, and worker protection. In evaluating the need to review EU legislation (REACH, waste legislation, air and water legislation, and worker protection), the Commission will pay particular attention to the issues suggested by the Parliament, and report on its conclusions from the review process referred to above. The Parliament's opinion also includes a number of specific requests to the Commission, related to certain aspects of regulation, labelling, ethics, the involvement of stakeholders, fact-finding, research and coordination.

The European Economic and Social Committee (EESC) also adopted an opinion on the regulatory review in its session of February 2009.²¹⁰ According to the EESC, a foresight for risk assessment of nanotechnology products should be developed, along with an integrated regulatory frame of reference and a joined-up system of governance at international level, to give clear, reliable and complete answers on the ethical impact, the possible risks for health and the environment, and possible developments in these areas.

The Commission has undertaken to present a new report in 2011, paying particular attention to a number of points raised by the European Parliament and the European Economic and Social Committee. In the light of the various actions mentioned in this section, the Commission also intends to present in 2011 information on types and uses of nanomaterials, including safety aspects.

6.2.2. Sectoral developments

The European Parliament and the Council have agreed on a recast of the Cosmetics Directive. In addition to the earlier pre-market authorisation of UV filters, colorants and preservatives, the new regulation introduces various provisions specific to other nanomaterials. These provisions include a notification obligation for manufacturers regarding the presence of nanomaterials in cosmetics not subject to prior authorisation; a possibility for the Commission to request a safety assessment for such materials by the Scientific Committee for Consumer Safety (SCCS); and a labelling requirement for nanomaterial ingredients. The new regulation

²⁰⁹ P6-TA-2009-0328,

<http://www.europarl.europa.eu/sides/getDoc.do?type=TA&language=EN&reference=P6-TA-2009-0328>

²¹⁰ 2009/C 218/04,

<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2009:218:0021:0026:EN:PDF>

introduces a definition of nanomaterials used in cosmetics ingredients. It also introduces an obligation on manufacturers to notify to the national competent authorities serious undesirable effects of products known to the manufacturers, or which should reasonably be expected to be known to them. The recast will formally be adopted, as a regulation, by the end of 2009.

In the context of discussions on a modification of the regulation on novel food, the European Parliament has proposed various provisions specific to nanomaterials. In particular, it is proposed to make it explicit that the use of nanotechnologies or nanomaterials for food and food ingredients already authorised will require a new authorisation. However, discussions continue as part of the second reading.

The introduction of provisions specific to nanomaterials naturally requires the adoption of a definition. The regulation on cosmetics and the new regulation on novel food therefore introduce a definition. However, in view of the various definitions of nanomaterials published by different bodies, and the constant technical and scientific developments in the field, the Commission is given a mandate to adjust these definitions in the light of technical and scientific progress, and to align them with definitions subsequently agreed at international level.

In the area of chemical substances, particularly relevant to nanomaterials, a specific group of competent authorities was created in March 2008, namely the REACH Competent Authorities Sub Group on Nanomaterials (CASG Nano), to discuss how REACH applies to nanomaterials. The objective is to exchange views on existing and future implementation issues, and other matters related to nanomaterials under REACH. On this basis, the group will provide recommendations to the REACH Competent Authorities, advising the Commission. Stakeholders are invited to participate in the meetings.

So far, three official meetings and an informal workshop have been held. The sub-group has established a work programme up to 2012, based on the implementation deadlines under REACH. The group issued its first paper “Nanomaterials in REACH”,²¹¹ endorsed by the REACH Competent Authorities meeting in December 2008. The group has also started a REACH Implementation Project on Nanomaterials, called RIPoN, to carry out further technical work on substance identification, information requirements and chemical safety assessment. This will allow research results to be integrated with the further adjustment of the REACH implementation guidance for specific aspects of nanomaterials.

The Commission will propose a review on the Seveso II Directive in 2010, to align its Annex I to the UN Global Harmonisation System (UNGHS). The Commission continues to follow carefully the issue of nanomaterials, also considering relevant research projects. The issue will be also addressed in OECD, in the project “Prevention of major accidents resulting from nanotechnologies” (included in the 2009-2012 Work Programme of the OECD Working Group on Chemical Accidents and OECD-WPMN).

In the Commission’s proposal for a Regulation concerning the placing on the market and use of biocidal products,²¹² active substances at the nanoscale are implicitly included in the term “active substances”. The proposed Regulation will repeal and replace the current Directive 98/8/EC concerning the placing of biocidal products on the market.

²¹¹ http://ec.europa.eu/enterprise/sectors/chemicals/reach/nanomaterials/index_en.htm,
<http://ec.europa.eu/environment/chemicals/nanotech/index.htm>

²¹² COM(2009)267 of 12 June 2009

The European Food Safety Authority (EFSA) has evaluated an application for the use of titanium nitride (TiN) nanoparticles in PET²¹³ bottles. The petition is based on the assumption that TiN nanoparticles do not migrate into food. EFSA concluded in November 2008 that there is no safety concern, as the substance does not migrate into food. The Commission is currently reflecting on the impact of the authorisation of this substance, taking into consideration relevant factors of Community law. EFSA also made a statement in 2008 related to an application of silver hydrosol: As the data submitted by the petitioner were insufficient to characterise adequately silver hydrosol for risk assessment, no opinion was produced. Finally, in 2007 EFSA gave an opinion on silicon dioxide in nanoparticle form for coating PET bottles. However, as legislation on coatings is within the competence of Member States, no action was taken by the Commission.

The European Medicines Agency (EMA), with its experts within the scientific committees (coordinated by the Innovation Task Force), continues to support applicants during the development of nanomedicines. A number of scientific and regulatory aspects warrant further scientific research and debate (e.g. the impact of nanopharmaceutical components on biological systems, definition and borderline products, and impact on the evaluation of innovative nanomedicines). Nevertheless, the pharmaceuticals regulatory framework allows for a scientifically well-defined and robust evaluation of benefit-risk balance, on a case-by-case basis, for each nanomedicine submitted to the Agency.

An *ad hoc* expert group on nanomedicines (including academic specialists and regulatory scientists) was established recently to provide specialist input on new scientific and regulatory issues emerging in the development of novel nanopharmaceuticals, and to assist the EMA in the review of guidelines, in order to identify any relevant gaps and further needs for guidance. In addition, the EMA continues to contribute to the international activities in the sector and is now in the lead of an informal international technical group, which was set up as an outcome of the regulatory meetings launched by the FDA in 2006. An international workshop focusing on scientific aspects of nanomedicine development and evaluation will be held at the EMA in April 2010.

The Commission strategy on health and safety at work for the period 2007-2012 recognises nanotechnology as an important area of work in the context of identifying emerging risks. In this context, the European Agency for Safety and Health at Work (EU-OSHA) published in 2009 a European Risk Observatory report on workplace exposure to nanomaterials. This report identifies priorities for future action, such as identification of nanomaterials; description of exposure scenarios; measurement of exposures to nanomaterials; efficacy of protective measures; *in vivo* studies for assessment of adverse health effects of nanomaterials; validation of *in vitro* methods; and methods for the characterisation of physicochemical properties.

The Commission is aware that discussions are taking place at national level in some Member States, regarding legislative initiatives on nanomaterials. However, so far, no draft regulation regarding nanomaterials has been notified to the European Commission under Directive 98/34/EC, which lays down a procedure for the provision of information in the field of technical standards and regulations.²¹⁴

²¹³ Polyethylene terephthalate

²¹⁴ Official Journal L 204 , 21/07/1998 p. 0037 - 0048

6.3. Safety concerns associated with the use of nanomaterials

According to the opinions of the EU Scientific Committees,²¹⁵ not all nanomaterials induce toxic effects. The Scientific Committees stress that the hypothesis that smaller necessarily means more toxic cannot be substantiated by the published data. However, certain health and environmental hazards have been identified for a variety of manufactured nanomaterials, indicating potential toxic effects. Long, non-degradable, rigid nanotubes (longer than 20 micrometres) have in several experiments been found to have effects similar to hazardous asbestos, causing inflammatory reactions for instance. Experiments also indicate that carbon nanotubes with these characteristics could induce a specific form of lung cancer, mesothelioma, which is also observed in relation to asbestos exposure. Whether such nanotubes would pose a risk for humans is not known but cannot be ruled out.

This means that nanomaterials are similar to other substances, in that some may be toxic and some may not, and some may be toxic only under certain exposure conditions. As there is not yet a generally applicable paradigm for the identification of potential hazards of nanomaterials, the Scientific Committees continue to recommend a case-by-case approach for the risk assessment of nanomaterials.

Scientific knowledge about health, safety and environmental (HSE) aspects of nanomaterials is a critical factor for the implementation of safety legislation. Therefore, research efforts have intensified over the last five years or so – at the EU level, in Member States and internationally. To develop a sound knowledge base, targeted actions to address HSE issues have been launched through the Research Framework Programmes and the Commission's Joint Research Centre, and international collaboration has been intensified.

As with ordinary chemicals, the risk assessment of nanomaterials depends on the identification of hazards and exposures. However, the science needed to test and measure hazards and exposures is more complex for nanomaterials than for ordinary chemicals. Their small size requires analytical tools with high resolution and precision. Their reactivity and tendency readily to undergo changes when in contact with surrounding media require careful characterisation of test samples and the use of experimental setups able to ensure reproducibility.

These basic scientific issues have constituted a major hurdle. Some years ago, conflicting experimental results that were hard to explain and interpret were not uncommon. The situation has greatly improved; in particular, progress has been made in understanding the interaction mechanisms of nanomaterials with biological systems, and in the areas of analysis and measurement. However, there are still considerable uncertainties and knowledge gaps in assessing the short- and long-term risks of different nanomaterials for human health and the environment. According to a recent study by the Institute of Occupational Medicine (IOM, April 2009),²¹⁶ based on an inventory of 260 research projects, the minimum amount of data required to make limited risk assessments was available for only three nanomaterials: carbon nanotubes (for health risks), and nano-titanium dioxide and nano-silver (for environmental risks).

At the request of the Commission, the EU Scientific Committees advise on the potential risks of nanomaterials and respective methodologies. Since 2005, the Commission has requested six opinions. The EU Scientific Committee on Emerging and Newly Identified Health Risks

²¹⁵ on Emerging and Newly Identified Risks (SCENIHR), on Consumer Products (SCCP) and on food and feed in the European Food Safety Authority (EFSA)

²¹⁶ <http://www.iom-world.org/research/nanoparticles.php>

(SCENIHR) has delivered four opinions on nanomaterials;²¹⁷ the Scientific Committee on Consumer Products (SCCP) has published one on nanomaterials in cosmetic products;²¹⁸ and the Scientific Committee of the European Food Safety Authority (EFSA) provided one opinion about potential risks of nanomaterials in food and feed.²¹⁹ Finally, the European Medical Agency (EMA) has published a concept paper on nanotechnologies,²²⁰ which it applies in its work.

6.4. Analysis of research on health, safety and environmental issues

This section builds on research results from European projects, including those described in section 1.3, and other research results, drawing conclusions regarding their use in risk assessment and management of nanomaterials. The next section presents the needs for further research, taking the knowledge gaps into account.

Progress has been made, and continues to be made, in the characterisation²²¹ and exposure assessment methods for nanomaterials, in toxicokinetics and genotoxicity testing with mammalian cells, and in the environmental behaviour of nanomaterials. Numerous *in vitro* studies have shown that some nanomaterials induce oxidative stress at high concentrations. However, there is not enough information for drawing general conclusions on the relationship between the physicochemical properties of nanomaterials and toxicity, either *in vivo* or *in vitro*. Recent research has also identified new concerns related to *in vitro* studies on protein fibrillation processes (both enhancement and retardation);²²² to potential hazards created by certain types of nanotubes;²²³ to the potential of some nanoparticles to act as carriers for other contaminants (“Trojan horse” effect);²²⁴ and to the potential for transfer across the food chain in environmental species.²²⁵

²¹⁷ The first SCENIHR opinion in 2006 addressed “The appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies” in general terms:

http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_003b.pdf

The second opinion in 2007 dealt with “The appropriateness of the risk assessment methodology in accordance with the Technical Guidance Documents for new and existing substances for assessing the risks of nanomaterials”:

http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_010.pdf

This was followed in late 2007 by an opinion on “The scientific aspects of the existing and proposed definitions relating to products of nanoscience and nanotechnologies”:

http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_012.pdf

²¹⁸ “Safety of nanomaterials in cosmetic products”:

http://ec.europa.eu/health/ph_risk/committees/04_sccp/docs/sccp_o_123.pdf

²¹⁹ The Potential Risks Arising from Nanoscience and Nanotechnologies on Food and Feed Safety:

http://www.efsa.europa.eu/cs/BlobServer/Scientific_Opinion/sc_op_ej958_nano_en.0.pdf

²²⁰ <http://www.emea.europa.eu/pdfs/human/genetherapy/7976906en.pdf>

²²¹ That is, the determination of properties

²²² Linse S, Cabaleiro-Lago C, Xue W-F, Lynch I, Lindman S, Thulin E, Radford S E, and Dawson KA, *Nucleation of protein fibrillation by nanoparticles*, PNAS, 2007, 104, 8691-8696

²²³ Poland C, Duffin R, Kinloch I, Maynard A, Wallace WAH, Seaton A, Stone V, Brown S, MacNee W and Donaldson K, *Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study*, Nature Nanotechnology, 20 May 2008

²²⁴ See, e.g.,

http://www.efsa.europa.eu/cs/BlobServer/Scientific_Opinion/sc_op_ej958_nano_en.0.pdf?ssbinary=true

²²⁵

-Holbrook RD, Murphy KE, Morrow JB, Cole KD, Trophic transfer of nanoparticles in a simplified invertebrate food web, *Nat Nanotechnol* 2008; 3:352-5;

-Fortner JD, Lyon DY, Sayes CM, Boyd AM, Falkner JC, Hotze EM, et al., C60 in water: nanocrystal formation and microbial response, *Environ Sci Technol* 2005; 39:4307-16;

-Bouldin JL, Ingle TM, Sengupta A, Alexander R, Hannigan RE, Buchanan RA, Aqueous toxicity and

6.4.1. Characterisation, metrology and reference materials

A number of available measurement and analytical methods are generally applicable at the nanoscale. However, these need to undergo formal validation and harmonisation, especially at low-nanometre resolutions. The area is research-intensive because of the many ambiguities in the work with nanomaterials. In this respect, and especially for specific nanomaterials, it is important to note that particle size distribution is not a fundamental property of the material being studied, but a temporary state of dynamic equilibrium between dispersion and agglomeration in suspensions or aerosols. This clarification will allow unambiguous interpretations of test and measurement results to be obtained, and boost their further use in guidance documents for the implementation of regulations.

If specific requirements regarding nanoparticle characterisation are to be imposed by regulation, this will entail an operational quality assurance system for laboratories. In this context, the activities of EU producers of reference materials are highly relevant. An increasing number of reference materials are becoming available, including those produced by the Commission's JRC.²²⁶ However, most of these reference materials are not certified, which means that they have to be upgraded to provide the level of confidence required for regulatory purposes, including formal laboratory accreditation.

The Commission gave a mandate to the European Standards Bodies (CEN/CENELEC/ETSI), inviting them to present a programme of standardisation needed to support the introduction to the market of nanomaterials and nanotechnologies (details are given in sub-section 4.4.4). CEN presented a programme in May 2008, providing an overview of ongoing activities and needs, which are highly relevant *inter alia* to risk assessment. The Commission has finalised a new mandate, including standardisation of characterisation and exposure measurement methods.

6.4.2. Potential human health hazards

First and foremost, it is essential to obtain a regular and extensive characterisation of the nanomaterial in question immediately preceding testing, to ensure the usefulness of the test results. It is further clear that this has to be complemented by an additional characterisation of the form of the nanomaterial that is actually being introduced into the test systems. This is to ensure that the test results are actually linked to the nanomaterial in question, rather than to an artefact, or to a degraded or further aggregated or agglomerated form that is substantially different from the form to be tested. This is also consistent with scientific opinions (SCENIHR, SCCP and EFSA).

In relation to human toxicology, substantial progress has been achieved within the OECD-WPMN as part of (i) reviewing the various test guidelines available;²²⁷ and (ii) guidance for sample preparation and dosimetry. In general, the OECD guidelines are applicable to investigating the health effects of nanomaterials with the important proviso that additional consideration needs to be given to the physicochemical characteristics of the material tested, including dosing. In some cases, there may be a need for further modification to the OECD guidelines. Preparation of samples and dose administration are critical considerations for the

food chain transfer of quantum dots in freshwater algae and *Ceriodaphnia dubia*, *Environ Toxicol Chem* 2008; 27:1958-63;

-Petersen EJ, Huang Q, Weber WJ Jr, Bioaccumulation of radio-labelled carbon nanotubes by *Eisenia Foetida*, *Environ Sci Technol* 2008; 42:3090-5.

²²⁶ <http://www.irmm.jrc.ec.europa.eu/>

²²⁷

http://www.oecd.org/departement/0,3355,en_2649_37015404_1_1_1_1_1,00.html

tests and therefore guidance has been developed on sample preparation and dosimetry for the safety testing of nanomaterials. The review mentioned here is consequently seen as a “living” document, highlighting the feasibility of various approaches and allowing for continuous updates, given the rapid developments in this area. The outputs of European and other research projects were combined in this work of reviewing test guidelines; preparing the guidance for sample preparation and dosimetry of nanomaterials for various test systems; and providing guidance for the sponsorship programme.

Because of the particular relevance of the inhalation route for exposure to nanomaterials, and the anticipated difficulties in assessing the effects of nanomaterials by this route, a document on “*Non-inhalation exposure methods for studies on the pulmonary toxicology of nanoparticles*” was produced for use within the OECD sponsorship programme. This also included results of *in vivo* tests from the EU-funded Nanosafe2 project. This document compares currently available exposure techniques for the inhalation route, including the advantages and limitations of inhalation tests and intra-tracheal instillation tests, from the viewpoint of pulmonary toxicology.

Current research on nanomaterial toxicity and associated mechanisms relies heavily on non-validated alternative testing methods that are not always used with standardised procedures. This leads to considerable uncertainties in the research results and their comparability. To address this problem, some research projects have developed standard operation procedures to ensure wider comparability of the results and the ongoing work in the OECD-WPMN supports these activities.

Some of the test guidelines for degradation and accumulation are not applicable to the testing of nanomaterials, while others are applicable with limitations or under specific test conditions. General guidance documents should therefore be developed for testing the fate and degradation of nanomaterials. It is also important to perform a detailed review of the OECD bioaccumulation methods.

6.4.3. *Potential exposure throughout the life cycle*

The various projects on occupational, human health and environmental exposure have made substantial contributions to guidelines on exposure assessment in workplaces, which are compiled in a recently published OECD-WPMN document:²²⁸

- Comprehensive, state-of-the-art documents with recommendations on the safe handling and use of manufactured nanomaterials and exposure control measures exist (e.g. ISO, BSI, ASTM), as well as guidance documents for measurement of exposure (parameters) or monitoring. For the time being, these documents recommend the implementation of a precautionary approach in the manufacture and use of nanomaterials, without being too restrictive.
- However, more specific data on the effectiveness of a larger variety of exposure control measures are needed, and therefore further work is in progress. Data should be forthcoming in the near future from the many projects in this area. It is essential that the data be collected and reported in a harmonised manner, in order to optimise their use. It should be realised, however, that exposures cannot currently be evaluated with respect to relevant limit values. To develop a more science-based guidance or regulations, the following stepwise approach is recommended:

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<http://www.oecd.org/dataoecd/36/36/42594202.pdf>

- First, “good practices” should be set for various generic tasks, e.g. transferring, mixing, filling, bag dumping, spraying, and so on. These might be either existing practices as acknowledged by experts, or mixtures of control measures considered to be practically achievable for theoretically defined exposure scenarios.
- Second, comprehensive descriptions of exposure scenarios, including control measures, should be documented. Information specific to particular contexts should be made available, for example by summarising it in “fact sheets”. To characterise these good practice scenarios, the next step would be to collect data with respect to exposure. The data should be collected using harmonised and appropriate sampling strategies and equipment, allowing their interpretation for various exposure metrics and exposure measures. Storage in a database should permit future analysis, for example with respect to the effectiveness of control measures. To ensure harmonised storage of exposure and contextual data, a framework should be developed and made available to organisations collecting this type of information.
- The final step would be a quantitative benchmarking of the good practice scenarios against other scenarios for similar operational units.

It is essential that future work on the possible exposure metric of surface area incorporate the surface chemistry. Future work on test filters and protective equipment should also focus on agglomerates.

6.4.4. *Potential ecotoxicity, environmental fate and behaviour*

Many of the general factors described in the context of toxicity (sub-section 6.4.2 above) also apply to ecotoxicity.

Research work has so far focused more on human toxicity than ecotoxicity. Practically no work has been done on the issue of secondary toxicity. Methodological difficulties exist with regard to testing, because commercial nanomaterials often present significant differentiation with regard to their labelled properties, leading to unreliable and irreproducible results. Moreover, the energy dependent uptake and the intracellular presence of nanoparticles pose the question of bioaccumulation, which is becoming increasingly important.

Regarding the verification of available test guidelines for ecotoxicity, it was concluded that the guidance on preparation, delivery, measurement, and metrology is currently inadequate for the testing of nanomaterials, although the basic ecotoxicological principles are applicable. On the other hand, the terminology used in the OECD test guidelines is not descriptive of, or specific to, the particulate or fibrous nature of nanomaterials. Terminology should be revised, both to make it more specific to nanomaterials, and to assure that test outcomes accurately reflect the potential environmental hazard of nanomaterials. The current state of knowledge concerning nanomaterial ecotoxicity and possible exposure routes precludes making specific recommendations as to the development of new test guidelines.

Local effects, such as local nutrient depletion or shading at the cellular level, are important factors in ecotoxicity test systems, in need of further investigation. Furthermore, current knowledge on specific interactions of nanomaterials within water is still limited, especially with regard to humic acids, and therefore the currently obtained PNEC values (predicted no-effect concentrations) are to be considered preliminary. A crucial step in making standard ecotoxicity test methods more reliable for nanomaterials is the collection of knowledge on the specific direct and indirect effects of nanomaterials. Hypothesis testing and the assessment of non-standard endpoints may play an important role in this process. In order to make progress

in closing knowledge gaps, there is the need to analyse different endpoints and consider the appearance of measurement artefacts and indirect effects.

Work on the fate of nanomaterials in the environment and behavioural aspects has only just started and results from projects should be available in the next two years or so. An exception concerns some simulation results related to the aqueous environment, which confirmed that the basic laws of colloidal science also apply to the stability of nanomaterials in suspensions and showed that natural organic matter stabilises nanomaterial suspensions in fresh water. These results also contributed to the guidance document for sample preparation and administration including dosimetry.

6.4.5. *Life cycle assessment (LCA) of nanomaterials*

Life cycle assessment is needed to ensure minimal environmental exposures, ensure that material loops are closed, and so on. LCA is a structured, internationally standardised method and management tool for quantifying the emissions, resources consumed, as well as environmental and health impacts, which are associated with products and services. LCA takes into account the product's full life cycle, from the extraction of resources, production, consumption and recycling, up to the disposal of waste.

The LCA process should also include economic, social and geographic aspects, as concluded at two different events, the Nanoforum Workshop²²⁹ and the joint EU-US LCA Workshop.²³⁰ This would also allow a more complete analysis of sustainability, including for example the scarcity of raw materials. There is a need for user-friendly guidance, including approaches suitable to SMEs, for commercialising nanotechnologies.

6.5. **Research on health, safety and environmental issues – Further priorities from a regulatory perspective**

In the Communication on regulatory aspects of nanomaterials of 2008 and its accompanying Staff Working Document (see section 6.2 above), a thorough analysis of research needs was made from the regulatory perspective. Since then, the SCENIHR and the Scientific Committee of EFSA have provided their opinions on potential environmental, health and safety aspects of nanomaterials, and on what further research and developments are needed.

It can be concluded from the results described in section 1.3 that European research, including that funded by the EU Research Framework programmes and that taking place at the Commission's JRC, has contributed substantially to the knowledge base on the potential risks of nanomaterials to the environment, human health and safety. This is especially the case in the fields of nanomaterial characterisation, exposure measurement including sampling strategies and mitigation, and hazard identification.

However, a number of fundamental knowledge gaps remain. It is also necessary to develop methods further, and to validate and harmonise various methodologies for characterisation, toxicity, ecotoxicity, exposure assessment and mitigation. Only then can the various guidance documents and implementing regulations for the safety of nanomaterials be updated on a sound scientific basis. Without validated and standardised methodologies, including proper

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http://www.nanoforum.org/nf06~modul~showmore~folder~99999~scid~483~.html?action=longview_publication&

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ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/lca_nanotechnology_workshopoct2006_proceedings_en.pdf

instrumentation, it is clearly impossible to ensure reliable and robust risk assessments of any substances – and nanomaterials are no exception to this basic rule.

Based on the results obtained from earlier and current studies, the following work is needed in specific areas of risk assessment, in the short-term (up to 4 years), the medium-term (5-8 years) and the long-term (9-11 years). These priorities are indicative and may have to be reviewed in the future.

6.5.1. *Measurement methods, reference materials and characterisation*

Short-term needs:

- To generate validated and harmonised methodologies (including performance criteria for the acceptance of test results), in the areas of characterisation, exposure assessment and hazard identification. There has already been progress in the development, validation and harmonisation of reliable methods to assess relevant properties (size, shape, surface area and surface chemistry); particle size distribution; and physicochemical and biological parameters of nanomaterials in various matrices, biological and environmental media, and under various conditions. Also relevant are the definition of the metrics most appropriate for hazard characterisation and exposure assessment, and the development of reference nanomaterials. It should finally be noted that several characterisation methodologies are available but not yet validated and harmonised.
- To convey information on characterisation, exposure assessment and hazard identification methodologies to potential end-users and boost the use of reference materials for quality control, calibration and validation tools. This notes the progress in making reference materials available (including certified reference materials), to underpin the development, validation and quality assurance of such methodologies.
- To address fundamental phenomena and biological interactions. Such results should inform the work on toxicity and ecotoxicity, as well as the development of reference materials (and studies into their homogeneity and stability). This notes the progress in the “basic” characterisation of nanomaterials in biological and environment media (with regard to particle size, surface characteristics, substances on particle surface, particle charging, agglomeration, de-agglomeration, kinetics, solubility, formulation, explosion characteristics etc).

Medium- to long-term needs:

- To develop more reference materials and certified reference materials, covering especially differences in shape and structure, surface area, charge and surface chemistry. Suitable reference materials must be provided to relevant projects. Reproducibility is a crucial issue and covers: (i) preparation (especially batch-to-batch variations); (ii) dispersions (e.g. without additives); and (iii) the stability of biological materials. In addition it is important to ensure that the reference material is relevant to the situation being tested and to the material in commerce. In achieving this, a harmonised methodology should also be put in place, to ensure the comparability and subsequent acceptance of test results, as well as the reference materials themselves.
- To develop and certify test aerosols for toxicity studies. The relevant requirements for these, in addition to the primary nanomaterials characterisation, are: (i) to describe nano-aerosol characteristics immediately after release using aerosol dynamic parameters and models; (ii) to assess characteristics of “aged” nano-aerosols in the typical size range for auto-agglomeration (20-200 nm), and the typical range for attachment to background

aerosol (less than 1 micrometre); and (iii) to study the toxicity of aged nanoaerosols (homogeneous and heterogeneous agglomerates, and agglomerate stability).

6.5.2. *Test methods for effects on human health*

In this area, one can build on the substantial progress made in the context of the OECD-WPMN sponsorship programme. This includes (i) the guidance for the preparation and administration of samples to test systems; and (ii) the conclusion that a number of available validated test methods and test schemes are suitable for detecting adverse effects of nanomaterials to human health, including acute and chronic toxicity.

Short-term needs:

- To integrate the information already available into existing guidance documents and boost their application through awareness raising activities.
- To develop further, compare and validate *in vitro*, *in vivo* and *in silico*²³¹ test methods and strategies, in order to speed up the adjustment of current test guidelines for nanomaterials and to enable a gradual shift towards alternatives to animal testing. This is required for existing as well as for new test methods and strategies.
- To investigate in greater detail the toxicokinetics, metabolism and excretion of nanomaterials, and their potential to cause adverse health effects.
- To develop an approach, including the calculation of mass from surface area, number concentration and size, allowing also for a link to historical data. To develop an approach for the building up of a toxicity paradigm between adverse short- and long-term toxicological impacts and individual or combined physicochemical parameters, such as mass, surface area, number concentration and size, allowing also for the link to historical data. To ensure that information on both the approach and the toxicity data is effectively transferred to the expert communities on human and workplace exposure.
- To perform additional studies on the potential hazards of nanofibres and nanotubes, building on the recently published ones. This work should also include investigations of the influence on observed effects of mechanical or chemical means to suspend nanomaterials for testing.

Medium- to long-term needs:

- To further develop, harmonise and validate alternatives to animal testing methods, including high throughput testing systems.
- To carry out studies on a range of endpoints, assessing and quantifying the fate of nanomaterials in the body, organs, tissues and cells. Additionally, possible intermediate deposition should be quantified.
- To study the acute and chronic impacts, including studies on potential bioconcentration, bioaccumulation or persistence of various nanomaterial varieties. Consequently, suitable approaches are required to allow such an assessment.

²³¹ In silico methods include databases, quantitative structure-activity relationships, and various molecular modelling approaches, machine learning, data mining, network analysis tools and data analysis tools that use a computer. In silico methods are primarily used alongside the generation of in vitro data both to create the model and to test it.

6.5.3. Test methods for environmental effects

In this area also, one can build on the progress already made in the context of the OECD-WPMN sponsorship programme. This includes (i) the guidance for the sample preparation and dosimetry to test ecosystems; and (ii) the conclusion that a number of available validated test methods and test schemes are suitable, after ensuring a proper sample administration, for detecting adverse effects from nanomaterials to the environment, especially related to their ecotoxicity, bioaccumulation, persistence and bioavailability.

Short-term needs:

- To integrate the information already available in existing guidance documents and boost their application through awareness raising activities.
- To develop further, compare and validate *in vitro*, *in vivo* and *in silico* test methods, and testing strategies, covering also degradation and accumulation, in order to speed up the adjustment of current test guidelines and to enable a gradual shift towards alternatives to animal testing. This is required for existing as well as for new test methods and strategies.
- To investigate further effects, including the underlining mechanisms of actions of nanomaterials and the affection of endpoints of nanomaterials related to their nano-specific reactions, when interacting with biological macromolecules and cellular structures, such as proteins and nucleic acids as demonstrated *in vitro* plus the classification of the type of tests.
- To develop an approach for the building up of a toxicity paradigm between adverse short- and long-term ecotoxicological impacts and individual combined to physicochemical factors such as mass, surface area, number concentration and size, allowing also for a link to historical data. To ensure that information on both the approach and the toxicity data is effectively transferred to the expert community on environmental exposure.

Medium- to long-term needs:

- To develop, harmonise and validate alternatives to animal testing methods, including high-throughput testing systems.
- To investigate further interactions in various environment media and species.
- To develop suitable approaches to studying the acute and chronic impacts for several varieties of nanomaterials, including potential bioconcentration, bioaccumulation or persistence in the environment.

6.5.4. Exposure information throughout the life cycle

Short-term needs:

- To validate and harmonise available methodologies related to spherical shapes of nanomaterials, and tackle the background issue as part of an overall monitoring strategy. This work should also generate qualitative and quantitative performance criteria for the development of future acceptance criteria for reliable tests including results. This should be based on progress made in exposure measurement, sampling, and the assessment and correction of background.
- To develop further a testing strategy for nanomaterials, including aerosols, for exposure assessment and for scenarios of primary release of nanomaterials in workplace air.
- To finalise the harmonisation of available simulation methodologies (including performance criteria for the acceptance of test results); and ultimately to fine-tune these for different applications, materials, uses and environmental species. This priority builds on

the first generation of simulation methodologies, addressing coating stability in relation to worker exposure and skin penetration.

- To develop models with suitable sensitivity, which can predict residual concentrations of free nanoparticles from release rates; and to implement such models in the current EU guidelines for environmental exposure assessment. These models should provide for robust extrapolation and also make allowances for the implementation of existing mitigation approaches.

Medium- to long-term needs:

- To develop suitable monitoring approaches and equipment for personal exposure. These should be readily applicable to existing or currently developed preparation and manufacturing techniques, and assess the effectiveness of personal protection equipment. This work should also include the development of harmonised and validated analytical methods to detect and measure ambient concentrations of free nanomaterials in various matrices.
- To satisfy the requirements in the previous indent, a testing strategy is needed for nanomaterials in the aerosol phase, including various shapes, to simulate scenarios of primary release of nanomaterials in workplace air.
- To allow for an effective use of the outputs from the needs summarised above, it is essential to (i) develop and validate model aerosol sources for relevant classes of release mechanisms and species for use in toxicological studies; (ii) develop different test aerosols for toxicological studies; and (iii) develop new or refine existing aerosol dynamic models for predicting nanomaterial evolution including their validation, sensitivity testing.
- To fine-tune existing simulation methodologies in relation to product stability related to worker exposure and skin penetration for other types or varieties of nanomaterials used in different applications and modelling other uses as well as possible effects of these in various environmental compartments including species.
- To develop and validate real-time sampling and measurement approaches for environmental and consumer exposure. These should allow an investigation of synergistic effects of mixed exposures and exposures from re-used and recycled products, and use various human and environmental biomarkers of exposure.

6.5.5. *Life cycle Assessment (LCA)*

Short- to long-term needs:

- To further adjust, validate and harmonise currently available guidelines for the life cycle assessment of nanomaterials and nanotechnology-based products, building upon results from completed and ongoing activities. To develop hands-on guidance for simplified LCAs for SMEs.

6.5.6. *Exposure mitigation*

Short-term needs:

- To collect information on existing mitigation approaches, and to optimise current approaches to safe preparation and manufacturing, by also boosting their application through awareness raising activities and uptake for future activities.
- To further refine existing mitigation approaches, by building on existing and newly developed exposure models including available and newly generated data.

- To communicate results effectively, in order to boost the adoption of mitigation approaches in industry and by other relevant stakeholders.

Medium- to long-term needs:

- To improve and develop new, effective and economically viable waste management, minimisation, recycling, handling, treatment and disposal technologies, approaches and tools for various nanomaterials and products containing these.
- To develop inherently safe and waste-free manufacturing processes for various nanomaterials.

6.5.7. *Environmental fate*

Short-term needs:

- To support the development of a categorisation of nanomaterials based on their environmental fate and behaviour.
- To generate information to develop an approach, including the calculation of mass from number concentration, surface area and size, allowing for a link to historical data.
- To finalise the harmonisation of available simulation methodologies (including performance criteria for the acceptance of test results); and ultimately to fine-tune these for different applications, materials, uses and environmental species. This priority is built on the first generation of simulation methodologies addressing coating stability, in relation to end-of-life assessment, bioavailability, bioaccumulation and fate, and the distribution of nanomaterials in aqueous environments.
- To perform a revision of the standard OECD methods for measuring solubility in water to accommodate the measurement of the rate of dissolution of nanomaterials in the natural environment.

Medium- to long-term needs:

- To develop modelling and extrapolation approaches that can address various scenarios with appropriate sensitivity by building upon available methodologies and data.
- To perform studies on soil systems, marine and terrestrial species including primary producers and combine these with work on the establishment of standard protocols for future testing.
- To assess the possible transfer of nanomaterials from environmental species into the food chain. This should include dietary studies and an assessment of the role, if any, of the interaction of nanomaterials with the available amount of feed for various animal species in different environmental compartments and other environmental contaminants. This is noting initial results pointing towards local shortage of feed for different animal species in the aqueous compartment.
- To perform specific dietary studies assessing the role of functionalised nanomaterials, which are consisting of coating fragments, since such fragments may have a substantial influence on the uptake and translocation of such functionalised nanomaterials within the body of different animals in various environmental compartments.

A longer-term objective in all areas of risk assessment above is to extend the work to various nano-objects, especially “*active*” nanomaterials, which are still in the embryonic research phase. Although such nanomaterials are still in the research phase, this will facilitate the progress from “*reactive*” research on environmental, health and safety issues towards “*anticipatory*” research. Moreover, it is demonstrating the implementation of the “*integrated*,

safe and responsible” principle for the development of nanotechnologies by equally contributing to their future societal acceptance.

6.5.8. *Networking and Infrastructure*

Progress has already been made in the networking of existing infrastructures, and the establishment of new networks, to ensure a cost-effective and efficient examination of health, safety, and environmental aspects of nanomaterials throughout Europe.

Short-term needs:

- To enhance current networks and infrastructures of different types, to make them more effective and efficient.

Medium- to long-term needs:

- To establish effective links between different networks and infrastructures in Europe, and also with relevant activities worldwide.
- To effectively connect research networks active on medical applications of nanomaterials with the networks active on environmental, health and safety research. This will also facilitate the progress from “reactive” research on environmental, health and safety issues towards “anticipatory” research.

6.5.9. *Strategic and Structural Development Needs*

- It is essential to capitalise on the results already available and arising from current methodologies and their further development, as described in section 1.3. Nevertheless, their validation and harmonisation should now be accelerated.
- Many promising but non-validated alternative methods to animal testing exist and are used for mechanistic studies of nanomaterial toxicity. However, their acceptance in the ECVAM validation process and their development into high-throughput testing processes requires further research, as well as the development and validation of standardised protocols.
- Environmental, health and safety research needs to be expanded, to match the production and marketing of new materials and applications of nanotechnology.
- A distinction should be made between innovative environmental, safety and health research on the one hand, and the collection of reference data and routine testing by industry and competent authorities on the other hand. Clearly, Research Framework Programme resources have to be used for breakthrough innovation – proposals that are not sufficiently innovative do not score high enough in the evaluation to be funded, no matter how important they may be.
- As the proper application of risk assessment and Life cycle Assessment (LCA) requires reliable and generally agreed databases, a mechanism should be established to use existing or establish new ones and adequately populate those. This need cannot be covered by bibliographic databases. The issues are how such data can be anonymised, aggregated and made publicly available; and how such a mechanism could benefit from proprietary data. Various approaches for anonymising and aggregating data are available and should be employed to the maximum possible extent.
- Particular focus should be given to the activities of OECD-WPMN and ISO, to further develop and validate test methods and standards. Regulation requires internationally harmonised and validated standards and methodologies. The active contribution of the Commission to this work is therefore essential. This work has been instrumental and should continue.

- Cooperation with Member States and international partners should continue, as it is essential in prioritising research needs, boosting synergies and using resources efficiently.
- Greater transparency about research and research results is needed. Research projects funded by public money should generate publicly available data.
- In accordance with the “integrated, safe and responsible” principle for the development of nanotechnologies, and the Commission’s Code of Conduct, EU-funded research should integrate safety aspects at the earliest possible stage in the development of applications and new “active” nanomaterials. This will facilitate the progress from “reactive” research on environmental, health and safety issues towards “anticipatory” research.

6.6. International cooperation – developing a common base of knowledge

The challenge of filling knowledge gaps calls for international collaboration, coordination and the sharing of information. There is also a need to obtain internationally harmonised standards and methods, building on the availability of various candidate methodologies. In particular, the OECD, ISO and CEN have become key forums in the generation of formally recognised methodologies in areas relevant to legislation. In the OECD, formally recognised test methods and test guidelines are being developed and work on exposure has been initiated. In ISO and CEN, work on formal standards and nomenclature is ongoing and the first terminology definitions have been released.²³² The European Commission and EU Member States put significant resources into these activities.

Collaboration with international partners within EU-funded research projects is actively supported and several projects have partners outside the EU. Coordinated calls are also organised with other countries, like the US. This collaboration extends to research on risk assessment.

6.6.1. OECD Working Party on Manufactured Nanomaterials (WPMN)

In Europe most test guidelines applicable under EU regulations are based on the work of the OECD. In 2006 the OECD established the Working Party on Manufactured Nanomaterials (WPMN), to promote international cooperation in the health, safety and environmental issues of manufactured nanomaterials. This is the main forum for international cooperation in this area, for example in the development of test methods needed for the proper implementation of regulation.

The Working Party is implementing its work through eight specific projects to further develop appropriate methods and strategies:

1. Development of a Database on Human Health and Environmental Safety Research;
2. Research Strategies on Manufactured Nanomaterials;
3. Safety Testing of a Representative Set of Manufactured Nanomaterials;
4. Manufactured Nanomaterials and Test Guidelines;
5. Co-operation on Voluntary Schemes and Regulatory Programmes;
6. Co-operation on Risk Assessment;
7. The role of Alternative Methods in Nanotoxicology; and
8. Exposure Measurement and Exposure Mitigation.

²³² CEN ISO/TS 27687:2008

A flagship activity is the so-called “sponsorship programme”,²³³ launched in November 2007: This pools resources from all the OECD Member countries and involved industries in an effort to perform tests on an agreed priority list of 14 commercially relevant nanomaterials on 59 different endpoints.²³⁴ The outcome of this programme is expected in the years to come and will serve as a very significant resource supporting the implementation of enhanced safety requirements. A key condition is to make tests comparable, given the involvement of many independent research institutions. For nanomaterials this is a significant challenge, as reference nanomaterials, measurement and dosimetry are still under continuous development. The OECD has acknowledged these shortfalls and developed a “Guidance manual for sponsors”,²³⁵ and guidance for sample preparation and dosimetry, which is being finalised. There is a close collaboration with the standardisation work of ISO. The programme will serve the following purposes:

- It will generate data about the 14 nanomaterials on 59 endpoints.
- It will assess the applicability of currently available test guidelines to nanomaterials.
- It will help to identify any new intrinsic property and thereby the need for new test methods.
- It will generate knowledge about alternatives to animal testing methods.

Testing strategies used in the Sponsorship Programme should primarily focus on the endpoints presented in the sponsorship guidance manual, and make best use of existing test methods (OECD test guidelines, ISO standards or equivalent). The sponsorship programme requests that the special characteristics of nanomaterials and their potential impacts at the cellular level should be taken into account. Specific attention should also be paid to tests which provide mechanistic information and information on metabolic pathways.

A specific focus is also given in the sponsorship programme to the development of non-animal and alternative methods. A specific steering group is focusing on alternative test methods and test strategies and their validation. A report presented to the WPMN in 2008 addressed the role of alternative methods, prioritisation schemes for test method selection, quality and good laboratory practice, validation and testing strategies. At this stage, however, it is not possible to make recommendations as to specific alternative approaches to be used for testing nanomaterials. It is not clear how information generated through alternative methods can be used (including the identification of unforeseen target organs and knowledge of biological mechanisms of action).

Turning to exposure to nanomaterials, the Steering Group on exposure assessment and mitigation (SG8) started its work recently, and five documents have been published so far:²³⁶

- “Report of an OECD Workshop on Exposure Assessment and Exposure Mitigation: Manufactured Nanomaterials”

²³³ Details on the OECD-WPMN Sponsorship Programme can be found on http://www.oecd.org/document/47/0,3343,en_2649_37015404_41197295_1_1_1_1,00.html

²³⁴ [http://www.oilis.oecd.org/olis/2008doc.nsf/linkto/env-jm-mono\(2008\)13-rev](http://www.oilis.oecd.org/olis/2008doc.nsf/linkto/env-jm-mono(2008)13-rev)

²³⁵ This guidance can be downloaded together with other related documents from the following website: http://www.oecd.org/findDocument/0,3354,en_2649_37015404_1_119663_1_1_1,00.html

²³⁶ All of these reports can be downloaded from the following websites:
http://www.oecd.org/findDocument/0,3354,en_2649_37015404_1_119820_1_1_1,00.html
http://www.oecd.org/findDocument/0,3354,en_2649_37015404_1_119666_1_1_1,00.html
http://www.oecd.org/department/0,3355,en_2649_37015404_1_1_1_1,00.html
http://www.oecd.org/document/53/0,3343,en_2649_37015404_37760309_1_1_1_1,00.html

- “Identification, Compilation and Analysis of Guidance Information for Exposure Measurement and Exposure Mitigation: Manufactured Nanomaterials”
- “Emission Assessment for Identification of Sources and Release of Airborne Manufactured Nanomaterials in the Workplace: Compilation of Existing Guidance”
- “Comparison of Guidance on Selection of Skin Protective Equipment and Respirators for Nanotechnology Workplace: Manufactured Nanomaterials”; and
- “Preliminary Analysis of Exposure Measurement and Exposure Mitigation in Occupational Settings: Manufactured Nanomaterials”.

Currently, SG8 works on a compilation of laboratory guidance, and started discussions on activities related to environmental and consumer exposure.

As regards the risk assessment methodologies, the report on the current situation is being finalised, as well as the report from the workshop of the Steering Group on Risk Assessment (SG6), including case studies on nano-silver, titanium dioxide and carbon nanotubes. The OECD-WPMN also assessed the situation in the voluntary reporting regimes in its Member Countries; and established a database on research projects on the HSE issues of nanomaterials.²³⁷

6.6.2. *International Organization for Standardization (ISO)*

The activities of the nanotechnology-related Technical Committees in ISO (TC 229) and in CEN (TC 352) were presented in sub-section 4.4.3. Of the forty documents developed by ISO/TC 229, the two that have already been published are relevant to the regulatory aspect. In 2008, a first CEN/ISO Technical Specification was released,²³⁸ defining such terms as nanoscale, nanoparticle, nano-object and nanotube. This document now sets an internationally agreed set of important, fundamental definitions for the area of nanomaterials. The second published document is an informative technical report on health and safety practices in occupational settings relevant to nanotechnologies.²³⁹ Among the other documents being developed in ISO/TC 229, about ten are related to the terminologies of different nanotechnology domains.²⁴⁰ The Commission (mainly the Joint Research Centre) is closely following the work in ISO and CEN.

In addition, ISO/TC 146 released a technical report on inhalation exposure characterisation and assessment of ultra fine and nanostructured aerosols in workplace atmospheres.²⁴¹ And in the particle characterisation group in ISO/TC 24/SC 4, the particular issue of nanoparticle size measurements and the required reference materials is considered.²⁴²

In the international metrology and pre-normative arenas, collaborative organisations have been set up between EU partners and non-EU countries, as described in sub-section 4.4.5. An example is VAMAS, the Versailles project on Advanced Materials and Standards, which feeds the outcome of its research into the ISO standardisation process.

²³⁷ http://www.oecd.org/document/26/0,3343,en_2649_37015404_42464730_1_1_1_1,00.html

²³⁸ CEN ISO/TS 27687:2008

²³⁹ ISO/TR 12885:2008

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http://www.iso.org/iso/standards_development/technical_committees/list_of_iso_technical_committees/iso_technical_committee.htm?commid=381983

²⁴¹ ISO/TR 27628:2007

²⁴² http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_tc_browse.htm?commid=47166

ISO has also received a number of important recommendations from a workshop in February 2008²⁴³ and these are now being pursued:

- enhance the development, efficacy, harmonisation and uptake of documentary standards broadly relevant to the field of measurement and characterisation for nanotechnologies;
- identify good practice and guidance documents covering the suitability and limitations of measurement and characterisation techniques for use with nanomaterials;
- ensure a greater dissemination, verification and validation of handling and testing protocols and related procedures by the broader community; and
- ensure that, in the area of nanomaterials characterisation, there is sufficient clarity in the identification of measurands related to several materials properties, including those corresponding to endpoints addressed by the OECD-WPMN Sponsorship Programme.

6.6.3. Cooperation on Implementation of Regulation

As described above, the main forum for international cooperation on the implementation of regulation is the OECD. The world community also works together within ISO, where in particular work on terminology will create a basis for a convergent approach in regulation and implementation world-wide.

In addition, nanotechnology and nanomaterials remain standing issues on the agendas of international forums. In particular there is a regulatory dialogue with countries such as the US, Canada, Australia and Japan. Several meetings took place between these countries on achieving a convergent approach towards meeting regulatory requirements, with a particular emphasis on the sectors of food, cosmetic products, pharmaceuticals and medical devices. Sectoral regulatory cooperation with various trading partners has been established for cosmetics (ICCR²⁴⁴), pharmaceuticals (ICH²⁴⁵) and medical devices (GHTF²⁴⁶).

Attention is also drawn to a project entitled “Regulating Nanotechnologies in the EU and US: towards effectiveness and convergence”.²⁴⁷ This benefited from a grant by the Commission, and was implemented by the London School of Economics and Political Sciences, Chatham House, Environmental Law Institute and The Project on Emerging Nanotechnologies. Its final report was presented in September 2009, in a series of conferences with stakeholders and authorities from US and Europe.

UNGHS is responsible for the global harmonised system for the classification, labelling and packaging of chemicals, including nanomaterials. Discussions on nanomaterials have been initiated in one of the expert committees. The group has however decided to await results from the OECD-WPMN before carrying out further work.

The Strategic Approach to International Chemicals Management (SAICM) is a broad policy framework for chemicals management programmes under a voluntary UN process. In its

²⁴³ ISO, IEC, NIST and OECD International Workshop on documentary standards for measurement and characterisation for nanotechnologies, NIST, Gaithersburg, Maryland, USA, 26-28 February 2008”

http://www.standardsinfo.net/info/livelink/fetch/2000/148478/7746082/assets/final_report.pdf

http://www.oecd.org/findDocument/0,3354,en_2649_37015404_1_119808_1_1_1.00.html

²⁴⁴ International Cooperation on Cosmetics Regulation

²⁴⁵ International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

²⁴⁶ Global Harmonisation Task Force (for medical device regulation)

²⁴⁷

http://www2.lse.ac.uk/internationalRelations/centresandunits/regulatingnanotechnologies/nano_home.aspx

second conference in May 2009, SAICM identified nanotechnology and manufactured nanomaterials as an emerging policy issue. Although duplication of efforts should be avoided, SAICM can provide an overarching frame in the long term and will reach a much broader group than the OECD (worldwide governments, industry and the NGO sector). The conference concluded that SAICM should focus on information exchange and on facilitating access to relevant information on nanotechnologies and manufactured nanomaterials, especially by different stakeholders in developing countries and countries with economies in transition. For example, REACH, in its Articles 118-120, provides detailed help and guidance on the exchange of data and information on HSE aspects.

7. INTERNATIONAL COOPERATION

A proper and efficient approach to nanotechnology and nanomaterials must take into consideration the international dimension, in terms of R&D, access to information and regulation. International cooperation, including collaboration in research but not limited to this, is now an integral part of the Commission's policy in all areas of the Action Plan. Throughout this staff working document, reference has therefore been made to work at the international level, and the following is meant as a summary of headings only:

- Collaboration in research (section 1.6), including research on HSE issues (section 1.3)
- The Third International Dialogue in 2008 on the responsible development of nanotechnology (sub-section 1.6.3)
- Cooperation on regulatory aspects, mainly but not exclusively through the OECD-WPMN (sub-section 6.6.1)
- Contribution to international standards, through ISO (section 4.4), including the area of risk assessment (sub-section 6.6.2)
- Participation in the work of OECD-WPN on the governance of nanotechnology (section 4.5)
- Access to data and research results (sections 1.6 and 6.6)

Annex 1: Degree of fulfilment of Commission Actions in Nanotechnology Action Plan 2005-2009

The following table gives an assessment, necessarily subjective, of the degree of fulfilment of each one of the goals identified for Commission action in the Nanotechnology Action Plan 2005-2009 (the original text for each goal is reproduced). The ratings given are: 3 – complete fulfilment, which does not preclude future work in this area; 2 – partial fulfilment, although much work has been carried out; 1 – relatively little progress.

| | |
|---|---|
| 1. RESEARCH, DEVELOPMENT AND INNOVATION: EUROPE NEEDS KNOWLEDGE | |
| a) Reinforce N&N R&D in the European Union's seventh framework programme for research, technological development and demonstration activities (FP7), and has proposed a doubling of the budget compared to FP6. Interdisciplinary R&D should be strengthened along the entire chain for knowledge creation, transfer, production and use; | 3 |
| b) Propose specific support to research in nanoelectronics under the Information and Communication Technology (ICT) priority of FP7. In line with the research agenda of the European Technology Platform on Nanoelectronics, this will stimulate industrially-relevant research in a technologically mature field, provide the foundation for the next generation of electronics and enable many new ICT applications, whilst drawing on complementary research in other thematic areas; | 3 |
| c) Boost support for collaborative R&D into the potential impact of N&N, in particular engineered nanoscale entities (e.g. nanoparticles), on human health and the environment via toxicological and ecotoxicological studies as well as developing appropriate methodologies and instrumentation for monitoring and minimising exposure in the workplace, including portable in situ measuring devices ¹⁰ ; | 2 |
| d) Foster the development of European Technology Platforms in order to implement a strategic R&D agenda for N&N sectors that are important for Europe's competitiveness e.g. in nanomedicine, sustainable chemistry or space (including the possibility of launching European Technological Initiatives). | 3 |
| 2. INFRASTRUCTURE AND EUROPEAN POLES OF EXCELLENCE | |
| a) Establish a map of existing European N&N infrastructure and explore ways of maximising its added value by the exchange of best practice. Special attention will be paid to the needs of industry, in particular, small and medium sized enterprises (SMEs) so to reinforce cooperation with and technology transfer from academic R&D teams to conceive advanced prototypes and validate them in industrially relevant environments; | 2 |
| b) Support transnational networking and integration of resources across universities, R&D organisations and industry as a means of assembling critical mass through 'distributed' poles of excellence e.g. via the Networks of Excellence and Integrated Infrastructure Initiatives instruments under FP6. Some areas of N&N R&D would particularly benefit from such integration include nanotoxicology and nanoecotoxicology, as well as nanometrology that would support EU competitiveness in this field. | 2 |
| 3. INTERDISCIPLINARY HUMAN RESOURCES: EUROPE NEEDS CREATIVITY | |
| a) Promote networking and disseminate best practices for education and training | 2 |

| | |
|---|---|
| in N&N. A dedicated workshop is taking place in 2005 and the proceedings will be widely disseminated; | |
| b) Explore how to best encourage the development of relevant supporting activities (e.g. cross-border thematic networks and other actions), in particular through its programmes and specifically the proposed new generation of education and training programmes after 2006; | 2 |
| c) Promote the creation of an 'interdisciplinary European award in N&N' that recognises scientific advances and entrepreneurship and/or progress in the area of safety and the environment, in line with the integrated and responsible approach. Sponsorship from industry and other interested organisations will be sought; | <i>Specific action deemed unnecessary, since nanosciences and nanotechnologies are taking an adequate share of generic activities</i> |
| d) Explore the possibility for dedicated N&N 'Marie Curie' actions (e.g. fellowships) that stimulate transnational doctorate-level programmes. Lifelong learning for researchers and engineers will also be promoted by actions aimed at disciplinary and/or sectorial mobility. Special attention will be paid to the participation of women and duly rewarding the hosting institutions. | |
| 4. INDUSTRIAL INNOVATION: FROM KNOWLEDGE TO THE MARKET | |
| a) Foster the industrial exploitation of R&D N&N by bringing together stakeholders to exchange best practice for the commercialisation of N&N. Special attention will be paid to the societal, political and psychological barriers to entrepreneurship in Europe e.g. the stigma of failure, as well as how to better facilitate agreement upon licensing arrangements between industry and R&D organisations / universities e.g. the 'Berliner Vertrag' or the Responsible Partnering Initiative; | 1 |
| b) Increase the industrial involvement in collaborative EU R&D projects for N&N as a means of promoting the transformation of traditional industries as well as the growth of knowledge-intensive SMEs and 'start ups'. Means of providing support for smaller prototype/demonstration projects at EU-level will be explored; | 3 (2 with regard to demonstration projects) |
| c) Support the creation of a web-based 'Digital N&N Library' to analyse the diverse landscape of N&N in Europe and to draw together data from a wide range of sources e.g. publications, patents, companies, market data, R&D projects, organisations; | 3 ²⁴⁸ |
| d) Support pre-normative R&D for N&N in synergy with the activities of European Standards Bodies. It will in particular invite proposals for Specific Support Actions for 'nanometrology' in FP6; | 1 ²⁴⁹ |
| e) Support the establishment of a N&N Patent Monitoring System e.g. by the European Patent Office (EPO) as well as the harmonisation of practices in the processing of N&N patent applications between patent offices such as the EPO, United States Patent and Trademark Office (USPTO) and Japan Patent Office (JPO). | 1 (2 with regard to monitoring, e.g. OECD) |
| 5. INTEGRATING THE SOCIETAL DIMENSION: ADDRESSING EXPECTATIONS AND CONCERNS | |

²⁴⁸ Work of ICPC NanoNet and ObservatoryNANO projects

²⁴⁹ The Nanostrand project carried out a fact finding mission, however, pre- and co-normative research is yet to be funded, as is pointed out in the report of CEN on the programming mandate.

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| a) Ensure that Community funded R&D in N&N continues to be carried out in a responsible manner e.g. via the use of ethical reviews. Possible ethical issues for N&N include e.g. non-therapeutic human enhancement, invasion of privacy due to invisible sensors. The integration of ethical concerns, innovation research and social sciences into N&N R&D will help build confidence in decision-making related to the governance of N&N; | 3 |
| b) Ask the European Group on Ethics in Science and New Technologies to carry out an ethical analysis of nanomedicine. This will identify the primary ethical concerns and enable future ethical reviews of proposed N&N R&D projects to be carried out appropriately; | 3 |
| c) Support studies and foresight activities into future N&N scenarios so to provide useful information about the possible risks to, and potential impact on, society. In the area of nanobiotechnology, synergy can be developed with a study that is being undertaken by the Commission at the request of the European Parliament to assess and conduct a cost-benefit analysis of biotechnology and genetic engineering; | 2 |
| d) Create the conditions for and pursue a true dialogue with the stakeholders concerning N&N. In support of this dialogue, special Eurobarometer (EB) surveys should study the awareness of and attitudes towards N&N across Member States. This will allow an assessment of the effectiveness of different approaches across Europe as well as providing 'early warning' of particular concerns; | 2 |
| e) Produce multilingual information material to raise awareness of N&N for different age groups building upon the success of pilot initiatives that have been launched by the Commission including films, brochures and other internet-based material; | 3 |
| 6. PUBLIC HEALTH, SAFETY, ENVIRONMENTAL AND CONSUMER PROTECTION | |
| a) Identify and address safety concerns associated with applications and use of N&N at the earliest possible stage. The Scientific Committee on Emerging and Newly Identified Health Risks has been requested to provide an opinion on the appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of N&N; | 2 |
| b) Promote safe and cost-effective measures to minimise exposure of workers, consumers and the environment to manufactured nanoscale entities. It will also support a wide range of studies (including epidemiological studies) to (i) evaluate current and future projected levels of exposure, (ii) evaluate the adequacy of current approaches to control exposure and (iii) launch appropriate initiatives, propose measures and/or issue recommendations; 20 See Treaty Articles 152 (health), 153 (consumers), and 174 (environment) 21 See Point 22 of Chapter 9 (p. 82) of the 2004 Report by UK Royal Society and the Royal Academy of Engineering " <i>Nanoscience and nanotechnologies: opportunities and uncertainties</i> " | 1 |
| c) Develop with Member States, international organisations, European agencies, industry and other stakeholders, terminology, guidelines, models and standards for risk assessment throughout the whole life cycle of N&N products. Where appropriate, risk assessment and management procedures will need to be adapted accordingly to ensure a high level of protection; | 2 |
| d) Examine and, where appropriate, propose adaptations of EU regulations in relevant sectors in light of the above paying particular, but not exclusive, | 2 |

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| attention to (i) toxicity thresholds, (ii) measurement and emission thresholds, (iii) labelling requirements, (iv) risk assessment and exposure thresholds and (v) production and import thresholds, below which a substance may be exempt from regulation, are typically based upon mass quantities. | |
| 7. INTERNATIONAL COOPERATION | |
| a) Intensify dialogue at international level with a view to adopting a declaration or a ‘code of good conduct’ for the responsible development and use of N&N. Industry shall be invited to adhere to these principles; | 2 (3 at EU level) |
| b) Address issues of mutual benefit at global level e.g. on nomenclature, metrology, common approaches to risk assessment and the establishment of a dedicated database to share toxicological and ecotoxicological as well as epidemiological data; | 2-3 |
| c) Support the creation of a free and open European electronic archive of N&N scientific and technical publications according to the principles set out in the OECD Declaration on Access to Research Data from Public Funding. | 3 |
| 8. IMPLEMENTING A COHERENT AND VISIBLE STRATEGY AT EUROPEAN-LEVEL | |
| a) Monitoring and overseeing the implementation of this Action Plan, its conformity and coherence with Commission policies (e.g. R&D, education and training, employment, enterprise policies, health and consumer protection), related initiatives throughout the Union and other relevant activities (e.g. the Commission’s Biotechnology Steering Committee), so to ensure maximum effectiveness; | 3 |
| b) Reporting on progress made with the Action Plan every two years to the Council and the European Parliament, making use of indicators, where possible. A revision of the Action Plan, if necessary, shall be envisaged; | 3 |
| c) Performing a range of activities so to accompany and foster a useful, beneficial, profitable and consensual exploitation and application of N&N in the EU e.g. via dedicated ‘horizon scanning’ activities, pro-active and responsive dialogue with the public and ad-hoc initiatives at international level. | 2 ²⁵⁰ |

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Some activities have been carried out, including sectoral innovation foresight. HSE activities led to a substantial concentration of nanotechnology applications mainly in health, electronics & energy fields. However, a real enhancement of exploitation and application has not been achieved.

Annex 2: Nanomaterials on the market

Stages that describe the readiness of nanotechnology solutions for the market can be characterized as (1) scientific discovery; (2) laboratory prototype; (3) industrial demonstration (pilot-line scale); (4) introduction to industrialisation (normal plant level); and (5) scaling up to mass production. The volumes of nanomaterials produced and handled vary considerably in each stage, and influence the assessment of potential exposure and potential impacts of nanomaterials to human health and the environment.

This table concerns stages (4) and (5) above, which are indicated by (I) and (S), respectively. It refers to materials effectively on the market.

Ae: aerospace; Au: automotive; Co: construction; El: electronics; EE: energy and environment; Mnf: manufacturing; Med: medical and pharmaceutical; OG: oil and gas.

LuxResearch, 2009 and 2008; NanoRoadSME, 2008; and ObservatoryNANO, 2009

| Nanomaterial | Description | Examples of applications in use in the core sectors |
|-----------------------|---|--|
| Ceramic nanoparticles | <p>Metal oxides (e.g. titanium dioxide, zinc oxide, iron oxide, etc)</p> <p>Metal sulphides and nitrides, and other inorganic compounds</p> <p>All can be coated with layers of polymers, surfactants, or other inorganic materials</p> | <p>Ae: Metal and composite coatings with ceramic nanoparticles for aerodynamic surface (I). Au: Cerium oxide NPs for fuel additives to increase fuel efficiency (I). Au: NP-coated interior parts to stand extreme heat and pressure (I). Au: NPs to enhance appearance and protect exterior (I). Au: Ceramic NP coatings prevent deposits and enhance fuel efficiency of engines (I). Co: Titanium dioxide NPs for UV resistant paints, self-cleaning, repel of water, dirt and contamination, non-stick and stable (I). Co: NPs are used in protective coatings for wood and floors, and could potentially add flame retardancy (I). Co: Odour remediation (S). Mnf: Ceramic NP coatings and less common nanomaterials enhance mould release and anti-icing (I). Co: Nanoporous aerogels for insulation (S).</p> |
| Metal nanoparticles | <p>Metal nanoparticles are most commonly silver, gold, aluminium or nickel</p> | <p>Silver for antibacterial, and other noble metals for healthcare (aluminium hips). Magnetic iron-based alloys for energy transmission. Light metals with superior mechanical properties (Al and Mg alloys, Ti and Ti alloys) for structural applications.</p> <p>Ae: Silver NPs embedded in supports and polymers as antimicrobials (S). Au: Catalytic converters (I). Co: Silver NPs on ceramic substrates or embedded in polymers as antimicrobials (S). Co: Nanostructured alloys render steel much stronger, together with carbon nanotubes (CNT) (S). Mnf: Silver NPs embedded in supports and polymers as antimicrobial (S). Mnf: Specially engineered NPs improve properties like flow and dispersion (I). Mnf: Coatings based on polymers and organic-inorganic particles to prevent crystallisation, fouling and corrosion (I) Mnf: Filtration solutions using hollow nanofibres, antifouling coatings (I) Med: silver NPs for medical instruments and fabrics as antimicrobials and drug carriers (S).</p> |
| Nanoporous materials | <p>Materials (e.g. silicon dioxide, carbon, aluminium oxide, various polymers, metals and silicon) with pores of 0-100 nm</p> | <p>Co: A low-density nanoporous aerogel for insulation (I). Zeolites (with a scaffolding made of silicon, aluminium, and oxygen) with pore diameters from 0.3-1 nm for various sectors of industry (S).</p> |
| Carbon nanotubes | <p>Single-walled nanotubes (SWNTs), generally about 1 nm in diameter</p> <p>Multi-walled nanotubes (MWNTs), diameter 5-100</p> | <p>CNT/polymer composites and foams with high electrical conductivity for applications in conventional cold cathode or polymer LEDs.</p> <p>Ae: CNTs for Cu replacement in wiring (I). Au: CNTs to prevent static build-up on fuel lines (S). Co: CNT to add strength to cement (S). El: Nanostructured devices for active cooling with highly conductive features to provide thermal contact (I). EE:</p> |

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| | nm Double-walled nanotubes (DWNTs) | CNTs embedded in epoxy for stronger wind turbine blades (with weight halved while doubling blade diameter) (I). Mnf: Sensors based on CNTs and nanostructured devices for monitoring (I). |
| Fullerenes and POSS (Polyhedral oligomeric silsesquioxane) | Fullerenes, 1 nm in diameter POSS made of silicon and oxygen atoms | Fullerenes used as fillers and in some cosmetics. El: Fullerenes for resists, anti-static packaging for semiconductor wafers, and nanoimprint lithography (S). |
| Other carbon nanomaterials | Carbon black, graphite, nanoherring, carbon based nanofilms, graphene Combination of C, Si, N, B, Ti, e.g. C_3N_4 , Si_3N_4 covalent carbides like SiC and B_4C and metallic carbides like TiC or LaC_2 | Carbon black for applications e.g. in car tyres, antistatic textiles, cosmetics, colouring. Nanographite for pigment production, as additive to rubber and plastic products, and as electrode materials for batteries, fuel cells and supercapacitors. Graphitic nanoherring catalyst support materials. Graphene can be used in electronic applications, such as transparent conductive films – or even transistors and sensors. Carbide nanofilms and nanocrystalline carbonfilms, e.g. “diamond-like carbon” (DLC). |
| Quantum dots | Nanosized crystals of semiconductor materials | Quantum dots can be used for diagnostics, bio-labels and next-generation solar cells. |
| Dendrimers | Dendrimers, 2 nm to 20 nm diameter | El: Nanoscale engineering and NPs like QDs and dendrimers boost LED output and enable precision optical elements (I). |
| Nanostructured materials | Nanometre-sized metal grains or layers of various materials | Ae: Nanostructured metallic alloys and nanoporous materials for stronger and lighter aircraft, reducing fuel consumption (I). Au: Nanostructured metals for lightweight and strong moulded auto parts (I). EE: Nanoscale electrodes for higher performance of rechargeable batteries (I). EE: Catalytic converters in cars (I). Mnf: Diamond nanocrystals and nanostructured metal composites for more durable industrial parts (S). |
| Nanowires | Metallic and semiconducting wires, <100 nm in diameter and many microns in length | Nanowires for smaller, faster microchips and memory devices, and also for displays, energy storage devices and sensors. Au: Memory technologies, electrical wiring, and interconnections (I). El: Nanostructured electrodes and NP electrode coatings for better consumer devices (I). El: Soldering and bonding at lower temperatures protects nearby components (I). |
| Nanopolymers | Nanostructured polymers and fibres (10 nm diameter) | Nanopolymers for applications in the transport and packaging industries. Nanofibers for filtration of air and liquids. |
| Bionanomaterials | Engineered biomolecules (oligonucleotides, peptides, proteins, and bioactive molecules) with size 0-1,000 nm | Co: Light-control materials (I). EE: New processes enable bio-based packaging materials to be made from waste or strengthened for longer usage (I). |
| Nanoencapsulation | Liposomes, micelles, solid lipids, polymersomes, emulsions, and silicon dioxide shells as encapsulators | Encapsulators improve solubility and bioavailability of ingredients, protect molecules from degradation, shield undesirable qualities like taste or smell, provide optical clarity, and improve the texture of cosmetic products. |
| Nanoclays | Nanoclays (layered platelets of clays, | Primarily as polymer additives: Ae: High-heat thermoplastics used for interiors may also |

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| | generally aluminosilicon dioxidete ceramic materials) | incorporate nanoclays (I). Au: Nanoclays for lightweight and strong moulded auto parts (I). Mnf: Nanoclays for flame retardant electrical cable claddings, metal nanocomposites for stronger cables (I). |
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Annex 3: List of Acronyms

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| CASG Nano | REACH Competent Authorities Sub-group on Nanomaterials |
| CEFIC | <i>Conseil Européen de l'Industrie Chimique</i> |
| CEN | European Committee for Standardisation |
| CENELEC | European Committee for Electrotechnical Standardisation |
| CIP | Competitiveness and Innovation Programme |
| CLP | (Regulation on) Classification, Labelling and Packaging (of substances and mixtures) |
| EC | European Commission |
| ECHA | European Chemicals Agency |
| ECVAM | European Centre for the Validation of Alternative Methods |
| EESC | European Economic and Social Committee |
| EFSA | European Food Safety Authority |
| EGE | European Group on Ethics in Science and New Technologies |
| EIT | European Institute of Innovation and Technology |
| ELS(A) | Ethical, Legal and Societal (Aspects) |
| EMA | European Medicines Agency |
| ENIAC | European Nanoelectronics Initiative Advisory Council |
| EPA | US Environmental Protection Agency |
| EPAA | European Partnership on Alternative Approaches to Animal Testing |
| EPO | European Patent Office |
| ERA | European Research Area |
| ERC | European Research Council |
| ESFRI | European Strategy Forum on Research Infrastructures |
| ETP | European Technology Platform |
| ETSI | European Telecommunication Standards Institute |
| EU-OSHA | European Agency for Safety and Health at Work |

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| FPN | Nth Framework Programme of the European Community for research, technological development and demonstration activities |
| HSE | Health, Safety and Environmental (issues) – also referred to as EHS (issues) |
| ICPC | International Cooperation Partner Countries |
| ICT | Information and Communication Technologies (in FP7) |
| IEC | International Electrotechnical Commission |
| IPR | Intellectual Property Rights |
| ISO | International Organization for Standardization |
| IST | Information Society Technologies (in FP6) |
| IUPAC | International Union of Pure and Applied Chemistry |
| JRC | (European Commission) Joint Research Centre |
| JTI | Joint Technology Initiative |
| JU | Joint Undertaking (e.g. ENIAC JU) |
| KBBE | Knowledge-Based Bio-Economy (in FP7) |
| KIC | Knowledge and Innovation Networks (of EIT) |
| NEST | New and Emerging S&T (in FP6) |
| NIEHS | US National Institute of Environmental Health Sciences |
| NIOSH | US National Institute for Occupational Safety and Health |
| nm | nanometre, 10 ⁻⁹ metres |
| NMP | Nanosciences, Nanotechnologies, Materials and New Production Technologies (in FP6 and FP7) |
| NoE | Network of Excellence |
| NSF | US National Science Foundation |
| OECD | Organisation for Economic Co-operation and Development |
| OECD-CSTP | OECD Committee for Scientific and Technological Policy |
| PRINS | Pan-European Research Infrastructure for Nanostructures |
| R&D | Research and Technological Development |

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| REACH | (Regulation on) Registration, Evaluation, Authorisation and Restriction of Chemicals |
| SCCP | Scientific Committee on Consumer Products (up to March 2009) |
| SCCS | Scientific Committee for Consumer Safety (from March 2009) |
| SCENIHR | Scientific Committee on Emerging and Newly Identified Health Risks |
| SICA | Specific International Cooperation Action |
| SME | Small and Medium Enterprise |
| SRA | Strategic Research Agenda (of ETP) |
| S&T | Science and Technology |
| STAIR | Standardisation, Innovation and Research |
| TC | Technical Committee (e.g. CEN/TC, ISO/TC) |
| UNGHS | UN Global Harmonisation System |
| USDA | US Department of Agriculture |
| VAMAS | Versailles Project on Advanced Materials and Standards |
| WPN | (OECD) Working Party on Nanotechnology |
| WPMN | (OECD) Working Party on Manufactured Nanomaterials |