European Commission

NanoData Landscape Compilation

Health

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EXECUTIVE SUMMARY

Background

New ways to diagnose and treat diseases are being sought to address the increasingly global societal challenge of achieving healthy and long life for as many as possible. In Europe, goals have been set to raise by two years the length of the average healthy lifespan of Europeans by 2020.

Cardiovascular disease, cancer and diabetes were responsible for more than 70% of deaths from non-communicable diseases globally in 2012. Infectious diseases are also one of the leading worldwide causes of death in adults and were responsible for 16% of all deaths in 2012. Neurodegenerative diseases are increasingly affecting the ageing populations of the more developed countries, currently costing approximately EUR 130 billion per annum for care for people with dementia in Europe. The socio-economic cost of dealing with these and other diseases is mounting as the population grows and ages – in diagnosis and treatment, in the quality of life of the sufferers, and those who care for them, and in losses to the economy. The five health sub-sectors selected for review in this project are those mentioned above – cancer, cardiovascular disease, diabetes, infectious diseases and neurodegenerative diseases[1].

This report offers a snapshot of the status of the environment for nanotechnology in the context of health. Analysis of that environment, trends in the data and the effects of European policies and actions on health nanotechnology will be reported in the NanoData Health Impact Assessment and are therefore not included in this report.

Role of nanotechnology

Nanotechnology is more and more becoming a useful tool in detecting and treating disease - from reducing infection transmission by using super-clean, nano-textured bactericidal surfaces, to implantable devices that for the localised delivery of drugs, and the potential for regenerative medicine techniques including implanted bioactive materials and stem cell mobilisation.

To support these developments, it is necessary to have a solid research base on health and nanotechnology; a robust development and commercialisation route for the results of research; and an industry that is capable of producing products that are wanted by healthcare professionals and the public alike.

Policies

National policies to support health nanotechnology tend to be generic at Member State level in that they may support nanotechnology within broad science and technology initiatives (e.g. Innovate UK in the United Kingdom which funds across the board including projects on health) or support it as a designated priority but usually do not single out health specifically (e.g. NanoNext in the Netherlands). Examples of nanotechnology initiatives in which health is specified include the Austrian NanoInitiative and the Germany Ministry for Education and Research's Action Plan Nanotechnology 2015, as well as activities by the Danish Council for Strategic Research (now replaced by Innovation Fund Denmark) and the French Agence Nationale de la Recherche (ANR).

European supports are concentrated in the EU RTD Framework Programmes (see below, EU R&D projects) as these have the greatest role in EU funding of nanotechnology R&D. Other policies include those for industry and for health. There is also a strong focus on the need for scrutiny of the use of nanotechnologies for health and medical purposes, including developing strategies to test the safety of engineered nanomaterials such as those used in some heart and cancer treatment applications. The European Standardisation Committee (CEN) has a dedicated technical committee for

[1] The information in this report on health and the five selected sub-sectors was obtained by the use of keywords. Keywords that were unique to each sub-sector and could therefore be used to identify publications, patents, projects, etc. were identified through literature search and discussions with experts. In addition to the keywords for the sub-sectors, words were identified that were either relevant to more than one sub-sector or to areas of health that were not encompassed in any of the sub-sectors. Thus, a set of data could be generated for health overall as well as for the five sub-sectors. In the report, data that is relevant to health but not specifically to any one of the five selected sub-sectors is identified as Other (OTH).

nanotechnologies, addressing health, safety and environmental aspects.

Globally outside of the EU, countries which have specified health nanotechnology as a priority within their policies and programmes at some point in the recent past include Russia (the medicine and biotechnology cluster within RUSNANO) and Iran (under its Iran Nanohealth Committee). Other countries include health nanotechnology as means of achieving national goals (e.g. China (in addressing healthy ageing in its Five-year Plan for S&T Development 2011-2015) and Japan (which, in its Fourth S&T Basic Plan 2011-2015, has moved away from designated priority technology areas to solution-oriented programmes)).

In terms of available data, this report tracks research and development activities through projects, publications and patents to products and markets in the context of the wider socio-economic environment.

EU R&D projects

For projects at the European level, nanosciences and nanotechnologies (NT) were first provided for at a significant level in FP6, taking about 10% of the budget (EUR 1,703 million for nanotechnology out of EUR 16,692 million for FP6) mainly under the headings of NMP (EUR 870 million), Information Society (EUR 346 million) and Life Sciences (EUR 54 million), as well as Human Resources and Mobility (Marie Curie Actions, EUR 219 million). Health nanotechnology gained EUR 415 million out of the EUR 1,703 million for nanotechnology, again predominantly in the areas listed previously, NMP, etc.

In FP7, nanotechnology funding has also been approximately 10% of total funding (EUR 4,661 million out of EUR 44,917 million for FP7) mainly for NMP (EUR 1,596 million), ICT (EUR 561 million) and Health (EUR 157 million). Human Resources and Mobility (Marie Curie Actions) takes a large proportion (EUR 580 million) as does the European Research Council (EUR 1,026 million). Health nanotechnology gained EUR 1,339 million, 29% of nanotechnology funding.

Throughout FP6 and FP7, the same five countries (DE, UK, FR, IT and NL) have received the highest proportions of health nanotechnology funding and together have taken over half of the total although 58 countries have engaged in some way.

Higher education establishments predominate (receiving 54% of funding), followed by research organisations (23% of the funding). SMEs have slightly stronger funding participation in health nanotechnology (14%) than for nanotechnology (12%) or FP overall (11%), perhaps reflecting the business model operating in the health sector (with many start-up and spin-off companies from research, companies that later get taken over or sell their intellectual property to larger enterprises).

In terms of individual organisations in the EU28, the countries of France (CNRS[2], CEA[3]), Germany (Max Planck[4] and Fraunhofer[5] Gesellschaften), the United Kingdom (Imperial College, the University of Oxford) and the Netherlands (Universities of Twente and Utrecht, as well as Philips Electronics NL BV) are strongly represented in the top 25, that also includes organisation from Spain, Sweden, Denmark, Italy, Ireland and Belgium. Switzerland is the strongest non-EU28 country (EPFL[6] and ETHZ[7]) and Israel is represented by Tel Aviv University and Technion.

Looking at companies alone, Philips (NL) is the only one of the top 25 to participate in more than ten projects in FP6 and FP7 and the list is dominated by SMEs (18 out of 25). Only three other top 25 companies participated in more than five projects, all of them SMEs. In terms of location, the countries of the large companies are the Netherlands, Germany (2), Denmark, France, Austria, and Switzerland. Participating SMEs are largely in France, Germany, the United Kingdom, Italy, Belgium and Ireland.

[2] Centre National de la Recherche Scientifique, the National Centre for Scientific Research www.cnrs.fr
[3] Commissariat à l'énergie atomique et aux énergies alternatives, the French Alternative Energies and Atomic Energy Commission www.cea.fr
[4] Max-Planck-Gesellschaft, the Max Planck Society www.mpg.de
[5] Fraunhofer-Gesellschaft zur Förderung der angewandten Forschung e.V. www.fraunhofer.de
[6] École Polytechnique Fédérale de Lausanne, the Swiss Federal Institute of Technology in Lausanne www.epfl.ch
[7] Eidgenössische Technische Hochschule Zürich, Swiss Federal Institute of Technology in Zurich www.ethz.ch

Publications

Publication data for health nanotechnology revealed that, of 1.8 million publications globally related to nano-science and –technology between 2000 and 2014, 200,000 (11%) were relevant to health. Of the five sub-sectors under consideration in this report, cancer was by far the most prevalent topic (28% of health nanotechnology publications), followed by cardiovascular diseases (5%), infectious diseases (4%), neurodegenerative diseases (3%) and diabetes (2%). All of the figures are lower than the proportions for health overall.

The strongest publishing countries in 2014 were China and the US, followed by India, Germany, Korea and the United Kingdom. Of the EU28, the strongest in publications in 2014 were Germany, the United Kingdom, Spain, France and Italy. Apart from Spain, these are the EU28 countries that are also strongest in FP projects. Looking at the top 50 organisations for publication output, the top half of the list is dominated by China with thirteen of the top twenty. European organisations are only found in the bottom half of the list and are led by University College London (UK), the University of Cambridge (UK) and the University of Copenhagen (DK). However, there has been no normalisation of the data to take into account factors influencing publication output, such as the number of researchers/technicians/students or the research budgets of the organisations. Publishing at a much lower level also takes place in companies with AstraZeneca, Bristol Myers Squibb and Merck being the leading three for publications in 2014.

Patenting

The strong presence of countries such as Germany, the United Kingdom, France, Spain and Italy continues as patenting patterns in the EU28 are reviewed (although patenting globally is greatly dominated by the US and its research-performing organisations). Using patenting families[8] as the measure, the top EU28 countries for health nanotechnology patenting between 1993 and 2011 both by filing country and by country of applicant were the United Kingdom, France and Germany. The top eleven EU28 countries were the same for patent filings[9] and for granted patents and were led by Germany, France and the United Kingdom. Globally, nine of the top ten organisations filing patents were in the US, the tenth being the CNRS in France,

France, Spain and Germany each have more than one organisation patenting in the top twenty EU28 & EFTA universities and public research organisations, but patenting numbers are low. In terms of EPO granted patents in the time period, the CNRS (FR) again ranks highest at third. There is one EU28 organisation each from France, Spain, Italy and the UK in the top 15, seven others being from the US. Patents granted at the USPTO are dominated by US organisations, just Spain (University of Seville) and France (CNRS) being represented in the top 15.

Company patenting is dominated by the US but the Netherlands (e.g. Philips), France (L'Oréal) and Germany (Schering) are in the top ten for patent filings. The leaders in the EU28 are the Netherlands (Philips) and Germany (Schering, Siemens, Philips, Bayer Schering Pharma and Hexal) with Ireland (Elan Pharma) and France (Guerbet) also being in the top 25 companies for filings. Many of the same names appear in patents granted, and also Chiesi Farma (Italy) and Cancer Research (UK). Cancer patents dominated health nanotechnology patent applications in 1993-2011 with almost five times as many as for infectious diseases and cardiovascular disease in second and third places respectively.

Employment and value added

Past estimates of employment in nanotechnology range from 1.8 to 2.2 million jobs globally by 2015. Using proxies for the sector, it has been estimated that the health nanotechnology sector in Europe may employ 75,000 in therapeutics and drug delivery and 39,000 in diagnostics and imaging – a total of 114,000 people (approximately 6% of the total for nanotechnology employment and one third of nanotechnology employment in Europe).

Similarly, total value added from European health nanotechnology therapeutics and drug delivery has been estimated at over EUR 12 billion while total value added from European health nanotechnology diagnostics and imaging has been estimated at EUR 4.4 billion. Of the total of EUR 16.6 billion, EUR 15.7 billion is expected to be from large firms and EUR 0.9 billion from SMEs.

[8] At the European Patent Office, US Patent and Trademark Office or World Intellectual Property Office
[9] Measured by number of patent families

Products and markets for health through nanotechnology

The global market for products in nanomedicine (nano-pharmaceuticals and nano-diagnostics) is expected to grow from over USD 200 billion in 2013 to over USD 500 billion in 2019 (a compound annual growth rate (CAGR) of over 16%), with pharmaceuticals responsible for the larger share but diagnostics showing the larger growth rate (growing from 11% to 22% of the total and from USD 25 billion to USD 116 billion between 2013 and 2019). The global market for nano-pharmaceuticals is forecast to grow at a higher rate (CAGR 14.5%) than pharmaceuticals in general (CAGR 5.5%).[10]

Of over 100 products identified as being currently on sale, over half (56%) are nano-pharmaceuticals (i.e. drug delivery) and 13% are synthetic bone and tooth materials. One third of the products (31%) are aimed at cancer applications and almost one fifth (19%) to counter infectious diseases. Products have been identified in areas including drug delivery (for cancer, cardiovascular, infectious disease and other applications); biomedical markers and detection (for cancer, cardiovascular and infectious disease applications); ferrofluids (for cancer and other applications); MRI contrast agents (for cancer applications); and surface disinfectants and antimicrobials (for infectious disease applications). Applications outside of the five sub-sectors include proteomics, synthetic bone, synthetic tooth enamel, transfection reagents, nano-porous membranes, and drug production and mixing systems. In terms of the types of nanotechnology involved, two types (nano-porous membranes and antimicrobials) employ thin films or coatings; drug production and mixing uses nano-devices; and the rest use nanoparticles.

The largest markets and market forecasts are seen in materials (hydroxyapatite for synthetic bone and tooth enamel, USD 1.1 billion in 2019) and for drug delivery (USD 214 million by 2019) and potentially in new areas such as quantum dots (USD 435 million in 2019 for biological reagents using quantum dots) and proteomics, albeit that these are areas of great uncertainty in terms of how research will progress, whether approvals will be given and to what extent cost will be a factor. For proteomics, the market for conventional arrays is forecast to grow to USD 8.2 billion in 2019 but it is hard to predict what share of the market nanotechnology will capture. [11]

The economic downturn is leading governments to try to reduce healthcare costs and many of the treatments that incorporate nanotechnology have premium pricing. Reimbursement of such high-cost drugs is becoming a significant hurdle for the growth of such markets. Some areas in which nanotechnology has been applied successfully (e.g. MRI contrast reagents) have suffered a drop in demand related to their high cost and the arrival of alternatives.

Regulation and standards

European regulations for nanotechnology are well-advanced with definitions and many regulatory documents. These cover health applications as either medical devices, pharmaceuticals or chemicals, as well as generically as materials and substances manufactured at the nanoscale. The setting of standards for nanotechnology and for medicines lies with the European Standardisation Committee (CEN) and with the International Organisation for Standardisation (ISO). While no documents have yet been published on nanotechnology by CEN, ISO has reported on nanotechnology vocabulary for diagnostics and therapeutics for healthcare. Other ISO documents are also of relevance e.g. those on implants, medical devices and health informatics.

Societal challenge and public attitudes

Health is inherently a societal challenge and the use of nanotechnology to address it is largely seen in a positive light by the public. Personalised healthcare and targeted treatments are attractive options that are becoming more and more available. Consultations with the public and surveys of their views indicate a positive attitude to the use of nanotechnology for cancer therapies and other serious medical applications, more so than for food packaging or foodstuffs, for example, which are other areas considered in which the public may come into contact with nanotechnology. Concerns remain among stakeholders that nanotechnology is continuing to be over-sold and that this may be creating unrealistic expectations. There are also concerns that nanotechnology may contribute most to diagnostics, leaving patients with a diagnosis but no treatment.

[10] BCC Research
[11] Ibid

1 BACKGROUND

The ability to measure and manufacture at the nanoscale is opening up many new avenues within industry and across society. Health is one in which nanoscience and nanotechnology can be applied, as many of the diseases that affect society, and the treatments and cures for them, inherently exist at the nanoscale. The influenza virus[12] and HIV have dimensions of between 80-150 nanometres (nm) while hepatitis is approximately 45 nm across. Antibodies, which protect us against disease, commonly have dimensions of 12nm while glucose (so important in nutrition) is smaller at under a nanometre (0.9nm).[13]

Nanotechnology is helping the research and medical communities in the discovery of the causes of diseases and the development of diagnostics and therapeutics. It is expected that nano-diagnostic techniques and nano-therapeutics will increasingly be able to contribute to our health and well-being, thereby helping to address the societal challenges of health, healthy living and healthy ageing. Opportunities for industry are arising in the production of effective monitors, diagnostics and therapeutics using nanotechnology, thereby supporting economic growth and European sustainability and competitiveness. As in many other disciplines, Europe has a strong research base in health and nano-science and -technology and also has a strong chemical and engineering industry base to complement that.

This report is a Landscape Compilation of facts and figures related to nanotechnology and health. It offers a snapshot of the status in 2015 of the environment for nanotechnology in the context of health. Analysis of that environment, trends in the data and the effects of European policies and actions on health nanotechnology will be reported in the NanoData Health Impact Assessment and are therefore not included in this report. This document reports on past and current policies and programmes for nanotechnology (in particular, but not exclusively, those relating to health); the outputs of research (projects, publications and patents) and how those outputs are used in the application of nanotechnology to health and medicine (products and markets). Being a landscaping of nanotechnology, it does not provide detailed analysis of the data or its trends or draw policy conclusions. The analysis of the data in this report will be fully presented in the Impact Assessment report that accompanies it. The Impact Assessment considers the policies and practices at European level to date (an ex-post evaluation) and looks at gaps in the policies and practices, concluding with a review of what actions could be taken to enhance nanotechnology for health in the future (an ex-ante analysis).

The report also excludes wider health-related issues. It does not, for example, talk about the use of nanotechnology in the vehicles related to healthcare, nor the details of its use in the electronic and computer-based systems that support healthcare. These topics will potentially be addressed in future reports on transport and ICT[14]. The report addresses the application of nanotechnology to neurodegenerative, cardiovascular and infectious diseases and to diabetes and cancer[15], the main areas of health in which nanotechnology is increasingly becoming important[16, 17].

The outline of this report is as follows:

- Introduction to healthcare issues and the role of nanotechnology;

[12] http://www.flucentre.net
[13] http://learn.genetics.utah.edu/content/cells/scale/
[14] Information and communications technologies
[15] These five sub-sectors were selected as being either the most important in terms of societal challenges or in terms of high level of potential for the application of nanotechnology.
[16] The information in this report on health and the five selected sub-sectors was obtained by the use of keywords. Keywords that were unique to each sub-sector and could therefore be used to identify publications, patents, projects, etc. were identified through literature search and discussions with experts. In addition to the keywords for the sub-sectors, words were identified that were either relevant to more than one sub-sector or to areas of health that were not encompassed in any of the sub-sectors. Thus, a set of data could be generated for health overall as well as for the five sub-sectors. In the report, data that is relevant to health but not specifically to any one of the five selected sub-sectors is identified as Other (OTH).
[17] Throughout the report, the term nanohealth may be used to encompass diagnostics and therapeutics with a nanotechnology component to them, or their development and manufacture. The abbreviations NT (nanotechnology) and HT (health nanotechnology) are also frequently used.

- Societal goals and challenges;
- Policies and programmes to support health nanotechnology;
- Research projects, the EU Framework Programmes;
- Publications in health nanotechnology;
- Patenting in health nanotechnology;
- Industry and nanotechnology for health;
- Products and markets for health through nanotechnology; and
- The wider environment for nanotechnology and health (regulation, environmental health and safety, communication and public attitudes).

The next section introduces the five health topics (health sub-sectors) and the role of nanotechnology in addressing them.

2 INTRODUCTION TO HEALTHCARE ISSUES AND THE ROLE OF NANOTECHNOLOGY

2.1 Introduction to healthcare issues

This report considers both communicable[18] and non-communicable diseases. WHO, the World Health Organisation, reports[19] that, of 56 million global deaths in 2012, over two-thirds (38 million, 68%) were due to non-communicable diseases (NCDs). In terms of absolute numbers, there was a rise in mortality from non-communicable diseases over the annual figures reported in 2008 (36 million out of 57 million i.e. 63%). A large proportion of these deaths occurred before the age of 60, during some of the most productive periods of life as noted by the WHO.

The leading causes of global non-communicable disease deaths in 2012 (see table below) were:

- Cardiovascular disease;
- Cancer;
- Respiratory disease, including asthma and chronic obstructive pulmonary disease; and
- Diabetes.

Table 2-1: Leading causes of global non-communicable disease deaths in 2008 and 2012

	2008		2012	
	Million Deaths	% of Total NCD	Million Deaths	% of Total NCD
Cardiovascular Disease	17.0	47	17.5	46
Cancers	7.6	21	8.2	22
Respiratory Diseases	4.2	12	4.0	11
Diabetes	1.3	4	1.5	4
Other	5.9	16	6.8	17
TOTAL	36.0	100	38.0	100

Of the six WHO regions, the European Region[20] is the most affected by non-communicable diseases (NCDs), with an estimated 8.6 million deaths anticipated in 2015, up from 8.1 million in 2004. The impact of the major NCDs (diabetes, cardiovascular diseases, cancer, chronic respiratory diseases and mental disorders) is equally alarming: taken together, these five conditions account for an estimated 86% of the deaths and 77% of the disease burden in the Region[21].

Non-communicable diseases are linked by common risk factors, underlying determinants and opportunities for intervention – high blood pressure, tobacco use, harmful use of alcohol, high blood cholesterol, overweight, unhealthy diets and physical inactivity - hugely increased by lifestyle and demographic changes and influenced by environmental factors.

[18] From the US Centres for Disease Control and Prevention, communicable diseases are listed as follows: mumps, measles, rubella, polio, tetanus, diphtheria, pertussis, haemophilus influenzae type B, rotavirus, hepatitis A, hepatitis B, meningococcocal disease, varicella, pneumococcal pneumonia and influenza (all of which can often be prevented using vaccines) and tuberculosis, syphilis, chancroid, gonorrhea, granuloma inguinale, lymphogranuloma venereum and leprosy. See http://www.cdc.gov/

[19] WHO Global Health Observatory figures (http://www.who.int/gho/en/ accessed January 2015) and http://www.who.int/nmh/publications/ncd_report2010/en/

[20] EU Member States plus Albania, Andorra, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Iceland, Israel, Kazakhstan, Kyrgyzstan, Monaco, Montenegro, Norway, Republic of Moldova, Russian Federation, San Marino, Serbia, Switzerland, Tajikistan, The former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Ukraine and Uzbekistan.

[21] "Prevention and control of non-communicable diseases in the European Region: a progress report" (WHO, 2014)

2.2 Role of nanotechnology by disease type

The role of nanotechnology for each of the five disease types under consideration in this project is presented here, after a summary of information on the disease. Further and more detailed information is provided in the Annex on the *Role of Nanotechnology by Disease Type*. The purpose of nanotechnology in products is also discussed in the later section on *Products and Markets*.

2.2.1 Cancer

Prevalence and mortality rates in Europe

On a global scale, cancer accounted for 8.2 million deaths in 2012. Europe comprises only one eighth of the total world population but has around one quarter of the global total of cancer cases. Cancer was the second leading cause of death in EU countries in 2011 accounting for 26% of all deaths, with lung cancer, colon cancer and prostate cancer being the main causes of cancer death among men while breast cancer, colon cancer and lung cancer were the main three causes of cancer death among women. In 2012, an estimated 2.7 million new cases of cancer were diagnosed in EU Member States, 54% (around 1.5 million) occurring in men and 46% (around 1.2 million) in women, with some 3.2 million new patients per year.

Large variations exist in cancer incidence across European countries.[22] Cancer incidence is highest in northern and western European countries with Denmark, France, Belgium and Norway registering more than 300 new cancer cases per 100 000 population in 2012. The lowest rates occur in some Mediterranean countries such as Greece, Cyprus, and Turkey, at around 200 new cases per 100 000 population. These variations reflect not only variations in the prevalence of risk factors for cancer but also national policies regarding cancer screening and differences in quality of reporting.

The role of nanotechnology in cancer diagnosis and treatment includes the possibility of combining imaging and drug carrier features, making for early diagnosis of diseases and revolutionising their therapy. Much of the activity of pharmaceutical companies in the US is around targeted nano-delivery of drugs and nano-therapeutics, making this the most advanced area of nanomedicine. In addition, many nano-features will be crucial prerequisites for implementation of personalised medicine and therapy or even treatment of chronic diseases. Nanotechnology is helping to target active compounds towards tumours (rather than subjecting patients to full-body or full-organ doses) and some of these can be heated using radiofrequency waves to enhance the treatment. Implantable devices can be used for localised delivery of drugs and bio-nano-sensors can be used to monitor the efficacy of therapies. In imaging, nanoparticles are used as tracers and contrast agents and for improved endoscopes and catheters. In the future, stem cell production may be enhanced through targeting with active nanoparticles.

2.2.2 Cardiovascular diseases

Cardiovascular diseases cover a range of diseases related to the circulatory system, including ischemic heart disease (IHD) (often referred to as heart attack and caused by the accumulation of fatty deposits lining the inner wall of a coronary artery, restricting blood flow to the heart) and cerebrovascular diseases (diseases that relate to problems with the blood vessels that supply the brain, such as strokes). Central and eastern European countries report the highest mortality rates from heart attacks; Japan, Korea and France are the OECD countries with the lowest rates. Across OECD countries, mortality rates from heart attacks in 2011 were 90% higher for men than women.[23]

Cardiovascular diseases were the leading cause of death in Europe in 2011, accounting for almost 40% of all deaths in EU countries. [24]

The role of nanotechnology for cardiovascular diseases includes its use for therapies via implantable devices (with modified nano-surfaces e.g. stents with a nano-coating) and for targeted drug delivery.

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[22] OECD (2014), Health at a Glance: Europe 2014 OECD Publishing. http://dx.doi.org/10.1787/health_glance_eur-2014-en

[23] Source: OECD (2013), "Mortality from cardiovascular diseases", in Health at a Glance 2013: OECD Indicators, OECD Publishing http://dx.doi.org/10.1787/health_glance-2013-7-en

[24] OECD (2014), Health at a Glance: Europe 2014, OECD Publishing. http://dx.doi.org/10.1787/health_glance_eur-2014-en

In the future, it may be used in regenerative techniques including implanted bioactive materials and stem cell mobilisation.

2.2.3 Diabetes[25]

Diabetes is a chronic disease that occurs either when the body does not sufficiently produce or when it cannot effectively use the sugar-regulating hormone insulin normally produced by the pancreas. The World Health Organisation estimated[26] that 1.5 million deaths were directly caused by diabetes in 2012. It is expected to be the 7th leading cause of death in 2030[27]. In 2014, 9% of adults suffered from diabetes globally. Of the 3.4 million deaths annually due to high blood sugar, almost half are in people aged under 70 and over 80% occur in low- to middle-income countries. The two most common forms of diabetes are early onset (Type 1, insulin dependent) and late onset (Type 2).

Approximately 60 million people in the European Region have diabetes, roughly 10% each of both men and women with the disease being slightly more prevalent in men. It is becoming more common in Europe among all ages, mostly due to poor lifestyle effects (increases in overweight and obesity, unhealthy diet and lack of exercise). Diabetes increases the risk of heart disease and stroke, can cause severe nerve damage in the feet leading to foot ulcers, infection and eventual need for limb amputation, commonly causes damage to the eyesight and potential, is one of the leading causes of kidney failure and overall it doubles the risk of death compared with the peer group without diabetes.

The role of nanotechnology in diabetes care is in the potential replacement of injections of insulin (for Type 1 diabetes) by non-invasive treatments such as nasal sprays and patches and the use of pills. The small size of nanoparticles can enable them to enter the body through the skin and be absorbed into the body without direct injection. It may be possible in the longer term to combine a nanotechnology based sensor of glucose levels with a dermal patch that releases insulin to the body when required. As with many pharmaceuticals, nano-coatings are being explored as offering slow- and/or targeted- release of therapeutics.

2.2.4 Infectious diseases

Causing sixteen percent of deaths worldwide annually, infectious diseases are the leading cause of death of children and adolescents, and one of the leading causes in adults.[28] Mainly occurring in low- to middle-income countries, many of these deaths are preventable or treatable. Infectious diseases include, for example, diarrhoea, cholera, influenza, mumps, measles, hepatitis, tuberculosis, syphilis, gonorrhoea and leprosy. Some figures are given below on the incidence, mortality rates and healthcare cost of just a few of these. There has been specific focus at European level on HIV/AIDS, malaria and tuberculosis in the Seventh Framework Programme for Research and Technological Development (FP7, 2007-2013).

Diarrhoea[29], a preventable and treatable disease, kills over three quarters of a million children under five every year. Globally, there are nearly 1.7 billion cases of diarrhoeal disease every year, many of which could be prevented by the provision of safe drinking-water and adequate sanitation and hygiene.

Cholera was reported[30] in all regions of the world in 2013, including 22 countries in Africa, 14 countries in Asia, 8 in the Americas and 2 in Europe. There were 2000 deaths from cholera, spread across 26 countries, with 65% of those deaths occurring in 17 countries on the African continent and 30% occurring across the Americas, the Dominican Republic and Haiti.

A study of estimated deaths from influenza in the United States covering the 31 flu-seasons from 1976 to 2007 reported[31] death figures of between 3,000 and 49,000 with, in general, 90% of deaths

[25] http://www.who.int/mediacentre/factsheets/fs312/en/
[26] World Health Organisation. Global Health Estimates: Deaths by Cause, Age, Sex and Country, 2000-2012. Geneva, WHO, 2014.
[27] Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med, 2006, 3(11):e442
[28] www.smartglobalhealth.org
[29] http://www.who.int/mediacentre/factsheets/fs330/en/
[30] http://www.who.int/wer No. 31, 2014, 89, 345-356
[31] http://www.cdc.gov/flu/protect/keyfacts.htm

occurring in the age range of 65 and over in industrialised countries. Worldwide, annual flu epidemics cause about 3 to 5 million cases of severe illness, and result in 250 000 to 500 000 deaths. For EU/EEA countries, a rough estimate gives an average of 38,500 influenza attributable deaths per annum[32] in a typical year. In Europe, the impacts of illness on healthcare costs and productivity are significant. It has been estimated[33] that "the implementation of a 100% vaccination rate programme for all risk groups in France, Germany, Italy, Spain and UK would require an additional EUR 1.52 billion but would result in estimated savings of EUR 39.5 million of reduced primary care visits and further savings of EUR 1.59 billion in reduced hospitalisations respectively in these countries".

HIV/AIDS has infected over 70 million people worldwide, about 39 million of them having died. 35 million people were living with HIV at the end of 2013, an estimated 0.8% of adults aged 15–49 years worldwide. Sub-Saharan Africa remains the most severely affected location, with nearly 5% of adults living with HIV (71% of the global total). An estimated 1.5 million deaths took place in 2013, a decrease of 22% from the 2009 figure and 35% fewer than at the peak in 2005. This improvement is being caused by improved access to antiretroviral therapy (ART) and a declining incidence of HIV infection.

With over 200 million new cases every year and one death from it every minute (660, 000 deaths in 2010), malaria is among the deadliest of diseases[34]. It is most prevalent in sub-Saharan Africa, the second most affected region being South-East Asia, particularly India. Preventative and treatment methods for malaria include long-lasting insecticidal nets, indoor residual spraying and artemisinin-based combination therapies (ACT) with rapid diagnostic tests also being of importance. Drug resistance, and particularly resistance to artemisinin, is of particular concern to those aiming to prevent and treat malaria.[35]

Tuberculosis[36] killed an estimated 1.5 million people in 2013, 360,000 of whom were HIV positive. In the same year, 9 million people developed the disease, more than half of them in the South-East Asia and Western Pacific Regions. 4% of cases occur in the European Region and, in western European countries, result in an average of one death per 100,000 population per annum. Tuberculosis (TB) is generally regarded as preventable. Incidence rates are declining fastest in the European Region, having peaked in 1999, but they are not currently on target to meet the Millennium Development Goal of a 50% reduction in prevalence by 2015 compared with 1990.

The role of nanotechnology in infectious diseases includes prevention through the use of bacteria-free nanomaterials for super-clean surfaces to avoid infection transmission and potentially for imaging to trace the path of infection and to help in the implanting of diagnostic and therapeutic materials within the body. Through the use of nanotechnology, sensors are being made more sensitive and the time for diagnosis (and therefore treatment) is being reduced, one current application of nanotechnology to infectious diseases. Time critical diagnostic information can be obtained more rapidly and immediate treatment given, with monitoring with immediate feedback becoming a short-term research and development objective (e.g. for bacterial or viral infections).

2.2.5 Neurodegenerative disease

Neurodegenerative disease in the EU [37]

Europe has a rapidly ageing population. Currently, 16% of the European population is over 65, and this figure is expected to reach 25% by 2030. Neurodegenerative diseases such as Alzheimer's and Parkinson's disease are debilitating and largely untreatable conditions that are strongly linked to age.

Neurodegenerative disease is an umbrella term for a range of conditions which primarily affect the

[32] http://www.ecdc.europa.eu/en/activities/sciadvice/_layouts/forms/Review_DispForm.aspx?List=a3216f4c-f040-4f51-9f77-a96046dbfd72&ID=394
[33] Vaccine, Volume 24, Issues 47–48, 17 November 2006, Pages 6812–6822, http://www.sciencedirect.com/science/article/pii/S0264410X06008954
[34] http://www.who.int/malaria
[35] http://www.who.int/malaria/media/world_malaria_report_2012_facts/en/
[36] http://www.who.int/tb/publications/global_report/en/
[37] Adapted from: http://www.neurodegenerationresearch.eu and http://ec.europa.eu/health/major_chronic_diseases/diseases/brain_neurological/index_en.htm

neurons in the human brain. These diseases are currently incurable, being debilitating conditions that result in progressive degeneration and / or death of nerve cells and causing problems with movement (called ataxias) and/or mental functioning (called dementias). Neurodegenerative diseases include Alzheimer's disease and other dementias, brain cancer, degenerative nerve diseases, encephalitis, epilepsy, genetic brain disorders, head and brain malformations, hydrocephalus, stroke, Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis (ALS or Lou Gehrig's Disease), Huntington's disease, prion diseases, and others.

Dementias are responsible for the greatest burden of disease with Alzheimer's representing approximately 60-70% of cases. Alzheimer's disease and related disorders affecting over 7 million people in Europe, and this figure is expected to double every 20 years as the population ages.

It currently costs approximately EUR 130 billion per annum to care for people with dementia across Europe, making age-related neurodegenerative disease one of the leading societal challenges faced by EU Member States. Alzheimer's disease is particularly expensive to manage due to its insidious onset, its ever-increasing levels of disability and the length of time over which the condition extends itself (average duration: 2 to 10 years).

Existing treatments for neurodegenerative diseases are very limited, and only treat the symptoms, rather than addressing the cause. Indeed, no new drug treatment for Alzheimer's disease has been approved in the past five years. Such diseases are highly complex and their origins remain unclear making diagnosis and treatment difficult. Given these challenges, it is hard to know where best to invest in research and development on early diagnosis and therapy so the focus is on management of the symptoms once the diseases appear.

Prevalence and cost of dementia in OECD countries[38]

Clinical symptoms of dementia usually begin after the age of 65, and the prevalence increases markedly with age. The disease affects more women than men. In Europe, 14% of men and 16% of women aged 80-84 years were estimated as having dementia in 2009, compared to less than 4% among those under 75 years of age. For people aged 90 years and over, the figures rise to 31% of men and 47% of women. A similar pattern is observed in Australia. Early-onset dementia in people aged younger than 65 years is rare; they comprise less than 2% of the total number of people with dementia.

The direct costs of dementia account for a significant share of total health expenditure in OECD countries, greater than the direct costs related to depression and other mental disorders such as schizophrenia. In the Netherlands, dementia accounted for nearly 6% of overall health spending in 2007. Most of these costs were related to caring for people with dementia in nursing homes, but part of the cost was also related to home-based care and a smaller proportion for hospital-based care. In Germany, dementia accounted for 3.7% of total health expenditure in 2008, with most of the costs also allocated for care in nursing homes.

The role of nanotechnology in the diagnosis and treatment of neurodegenerative diseases is potentially the strongest in the use of semi-invasive devices for drug delivery, implantation of advanced neuro-stimulators using nano-enhanced imaging techniques and the possibility of combining imaging and drug carrier features, making for early diagnosis and targeted therapy. More personalised treatment would become possible if nanotechnology, biotechnology and engineering can be combined to measure a patient's genetic predisposition to side effects and their drug response characteristics. Less intrusive and miniaturised devices can offer enhanced acceptability in patients, an advantage perhaps particularly relevant to people suffering from neurodegenerative diseases and other neurological conditions. Further in the future, nanotechnology may contribute to site-specific delivery of neuro-active molecules and techniques for regeneration of the central nervous system.

[38] OECD (2013), "Dementia prevalence", in Health at a Glance 2013: OECD Indicators, OECD Publishing. http://dx.doi.org/10.1787/health_glance-2013-74-en

The ten leading causes of death in the world, 2000 and 2012 (WHO, 2014)[39]

Ischaemic heart disease, stroke, lower respiratory infections and chronic obstructive lung disease have remained the top major killers during the past decade.

HIV deaths decreased slightly from 1.7 million (3.2%) deaths in 2000 to 1.5 million (2.7%) deaths in 2012. Diarrhoea is no longer among the five leading causes of death, but is still among the top ten, killing 1.5 million people in 2012.

Chronic diseases cause increasing numbers of deaths worldwide. Lung cancers (along with trachea and bronchus cancers) caused 1.6 million (2.9%) deaths in 2012, up from 1.2 million (2.2%) deaths in 2000. Similarly, diabetes caused 1.5 million (2.7%) deaths in 2012, up from 1.0 million (2.0%) deaths in 2000.

Nanotechnology in health outside of the five selected sectors

Nanotechnology occurs in health in a wide range of applications (current and potential) that are not specific to individual disease types. For example, it has a role in surgical methods, implants, prosthetics, tissue engineering and tissue repair, as well as many generic drug delivery mechanisms, drugs, diagnostics and imaging techniques and equipment.

Also omitted are maternal, neonatal and nutrition conditions which collectively were responsible for 23% of global deaths in 2012, the same year in which injuries caused 9% of all deaths[40].

The category "Other" is used in this report for health nanotechnology that is not specific to the five disease sub-sectors under consideration.

[39] http://www.who.int/mediacentre/factsheets/fs310/en/
[40] www.who.int

3 SOCIETAL GOALS AND CHALLENGES

Health is inherently a societal challenge and both good health and long, healthy living are societal goals. Some health targets have been encapsulated in the Millennium Development Goals – to combat infectious diseases such as HIV/AIDS and malaria and to reduce child mortality through prevention (e.g. vaccines against diseases such as measles) and cure (for infectious diseases such as diarrhoea).

In the EU to 2020[41], five specific targets have been set (for employment; research and development; climate change and energy sustainability; education; and fighting poverty and social exclusion) but no specific goals for health. However, living long and healthy lives is a European priority. Health-related goals are included, for example, in one of the European Innovation Partnerships (EIPs), the EIP for Active and Healthy Ageing:

- improving health and quality of life (with a focus on older people);
- ensuring health and social care systems are sustainable and efficient in the long term;
- enhancing the competitiveness of EU industry through business and expansion in new markets

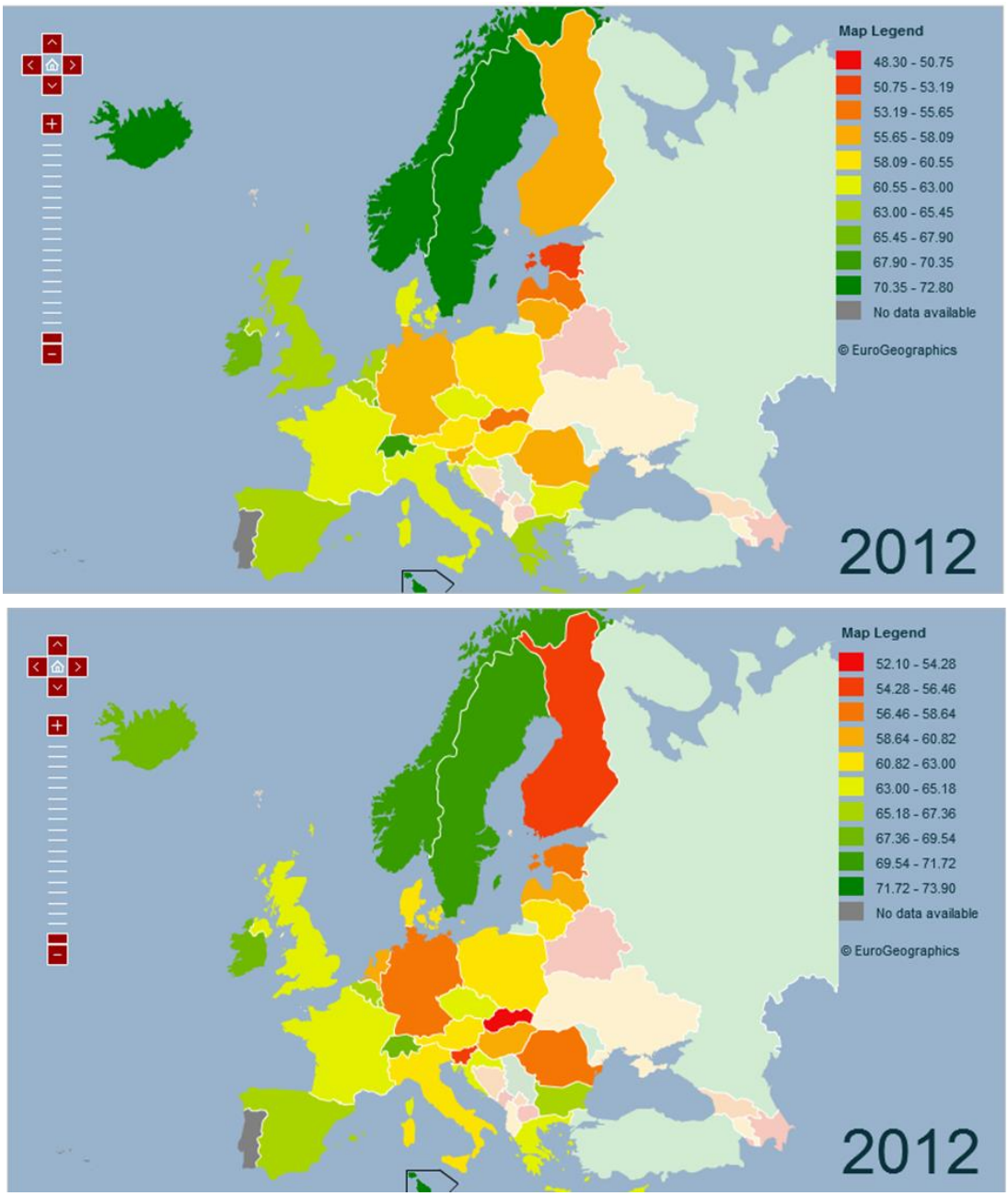
in order to increase the average healthy lifespan of Europeans by two years by 2020[42].

The goal of the EIP is measured as an increase in Healthy Life Years (HLY), i.e. years that a person of a certain age can live without disability. HLY is used to monitor health as a productivity and economic factor, combining the concept of quality of life and the concept of length of life (life expectancy). Currently, the average number of Healthy Life Years at birth in the EU is shorter than the average life expectancy (by 15 years for men and 20 years for women). There are substantial differences between countries, as seen in the figure below.

Changes in Healthy Life Years can have large implications, both in health care costs and in pension costs. Increasing age and life years spent in poor health result in greater medical needs in particular with regard to degenerative vascular diseases, cancer, and Alzheimer's and other neurodegenerative diseases. If the retirement age is to be raised, people must be physically able to work and enjoy healthy life years.

The Heidi data tool[43] presents comparable information on health at the European level. It includes various indicators on demographic and socio-economic factors; health status; determinants of health; and health interventions: health services.

[41] http://ec.europa.eu/europe2020/europe-2020-in-a-nutshell/targets/index_en.htm
[42] http://ec.europa.eu/health/ageing/innovation/index_en.htm
[43] http://ec.europa.eu/health/indicators/indicators/index_en.htm



Source: The Heidi data tool, http://ec.europa.eu/health/indicators/indicators/index_en.htm

Figure 3-1: Healthy Life Years at birth, 2012
Data for Men (top figure) and for Women (bottom figure)

The next section looks at support for public sector research and development (R&D) in the European Union, policies and programmes.

4 EU POLICIES AND PROGRAMMES FOR NANOTECHNOLOGY AND HEALTH

Support for public sector research and development (R&D) in the European Union is funded by Member States either directly through national programmes or indirectly via the programmes administered by the European Commission and its agencies. In addition, research and development is funded by companies (intra- and extra-mural R&D) and by philanthropic bodies and individuals. This report concentrates mainly on funding via the European Commission (EU funding), Member State funding and the outputs of industry funding of its own R&D[44].

EU funds for research and innovation are provided through dedicated programmes. In 2014-2020, these include the Framework Programmes (formerly the Seventh Framework Programme (FP7), currently Horizon 2020), covering all research fields and fully dedicated to funding research and innovation activities; sectoral research programmes (nuclear energy, coal and steel, space); and the European Structural and Investment Funds. These programmes are complemented by five other EU programmes with links to research and innovation activities: The Third Health Programme[45], Life[46], Erasmus+[47], COSME[48] and the Connecting Europe Facility[49].

This section will first examine the EU Framework Programmes.

4.1 The EU Framework Programmes: supports for nanotechnology

The Framework Programmes being the largest source of EU funds for R&D, they have the greatest role in EU funding of nanotechnology R&D. Support specifically named as being for nanosciences and nanotechnologies was first provided at a significant level in the Sixth Framework Programme (FP6, 2002-2006) [50]. The NMP (Nanotechnologies and nanosciences, knowledge based multi-functional materials and new production processes and devices) had the largest number of health nanotechnology projects and over 50% of the total FP6 health nanotechnology funding.

Nanotechnology funding in FP6 was followed up with targeted funding in the Seventh Framework Programme (FP7, 2007-2013), the largest part specific to nanotechnology being the "Nanosciences, Nanotechnologies, Materials and new Production Technologies (NMP)" theme under the Co-operation Programme. Once again, this specific activity for nanotechnology has played the most significant role in supporting nanotechnology research. EUR 3.5 billion have been allocated for NMP over the duration of FP7 with the emphasis on:

- Nanosciences and nanotechnologies - studying phenomena and manipulation of matter at the nanoscale and developing nanotechnologies leading to the manufacturing of new products and services;
- Materials - using the knowledge of nanotechnologies and biotechnologies for new products and processes;
- New production - creating conditions for continuous innovation and for developing generic production 'assets' (technologies, organisation and production facilities as well as human resources), while meeting safety and environmental requirements; and

[44] There are also several philanthropic bodies that include in their interests a specific focus on health (e.g. the Gates Foundation[44]) but they are mainly US based and not specific to nanotechnology. There are also many voluntary organisations addressing cancer, various ageing and neurodegeneration issues and heart conditions but they have limited funding and very specific policies (e.g. the Alzheimers Foundation, the Heart Foundation, Macmillan Cancer Support, etc.).

[45] Preventing diseases, protecting EU citizens from cross-border health threats, contributing to innovative health systems, and facilitating better access to healthcare.

[46] For environment, biodiversity and climate change.

[47] Supporting relocation for education and training purposes.

[48] Supporting the creation and expansion of companies, especially by expanding their research and innovation activities.

[49] Improving trans-European infrastructure for transport, energy and telecommunications.

[50] FP6 NMP: Nanotechnologies and nanosciences, knowledge-based multifunctional materials and new production processes and devices: thematic priority 3 under the 'Focusing and integrating community research' of the 'Integrating and strengthening the European Research Area' specific programme, 2002-2006.

- Integration of technologies for industrial applications - focusing on new technologies, materials and applications to address the needs identified by the different European Technology Platforms (see also below).

There are many other initiatives under FP7 (with less budget for nanotechnology than NMP) that can fund R&D on nanosciences and nanotechnologies including those for ICT, health, energy, transport and the environment. These topics are also funded under other programmes within EU funding but the Framework Programme remains the largest designated source of R&D budget. Within FP7, non-specific basic research, People and Capacities are funded (in addition to the Co-operation Programme) and each of these provides potential funding for nanoscience and technology. Significant examples of these are:

- The European Research Council (ERC): total funding of up to EUR 7.5 billion in FP7 (and EUR 13.1 billion in 2014-2020 under Horizon 2020[51]) for investigator-driven, bottom-up research ideas in science, engineering and interdisciplinary research, awarded through open competition;
- The Marie Curie Actions[52]: total funding of up to EUR 4.7 billion FP7 in 2007-2013 (and EUR 6.16 billion Horizon 2020 funding in 2014-2020) for training, mobility and career development of researchers; and
- The Capacities Programme[53]: total budget of EUR 4.1 billion, funding for research infrastructures; research for the benefit of SMEs; regions of knowledge and regional research-driven clusters; research potential of Convergence Regions; science in society; support to the coherent development of research policies; and international co-operation.

Framework Programme funding is covered in much greater detail later in this chapter.

Other mechanisms for collaboration on nanotechnology and ICT include the ERA-NETs, Networks of Excellence and ESFRI, as outlined below. Later in the report, there is coverage of EUREKA's Eurostars; the European Technology Platforms; and the Joint Technology Initiatives (and Joint Undertakings).

The ERA-NET scheme began under FP6 to support collaboration between and co-ordination of national research programmes and included a network on nanomedicine, EuroNanoMed[54] (European Network of Transnational Collaborative RTD Projects in the Field of Nanomedicine). EuroNanoMed (2009-2011) co-ordinated three joint calls across ministries and funding agencies, resulting in 24 projects with a total funding of EUR 46 million. The initiative is continuing as an ERA-NET in the form of EuroNanoMed II which will run until 2016, with 20 partners from 17 countries.

Pooling of Member State resources and collaboration to address common issues has also taken place through the Joint Programming Initiatives (JPIs). In these, Member States agree to create a partnership with common goals and a single strategic research agenda to address major societal challenges. In the context of health research, the Joint Programme on Neurodegenerative Diseases (JPND) is the most significant. Through the co-ordination of investment in research, the JPND is working to identify the causes of NDGs and to develop treatments, cures and care systems. Several partners in JPND are working on detection and treatments using nanotechnology (e.g. the NADINE[55] project on NAnosystems for Early DIagnosis of NEurodegenerative disease, and the ERA-NET Neuron[56]).

European research is also being strengthened through collaboration on the development, establishing and running of large research infrastructures, so large that they cannot easily be funded by one agency or country alone. Under the auspices of the European Strategic Forum on Research Infrastructures (ESFRI)[57], Member States are coming together to fund infrastructures related to health and other fields. EU grants support the preparatory phases of all selected projects and assist

[51] http://erc.europa.eu/
[52] http://ec.europa.eu/research/mariecurieactions/ Marie Curie Actions became Marie Skłodowska-Curie Actions under Horizon 2020.
[53] http://ec.europa.eu/research/fp7/index_en.cfm?pg=capacities
[54] http://www.euronanomed.net/
[55] http://www.fp7nadine.eu/
[56] http://www.neuron-eranet.eu/
[57] http://ec.europa.eu/research/infrastructures/index_en.cfm?pg=home

in implementation and operation of prioritised projects. The EU funding was EUR 1.85 billion in FP7 and is about EUR 2.5 billion in Horizon 2020. Research infrastructures relevant to health include the Biobanking and BioMolecular Resources Research Infrastructure (BBMRI)[58] and European Clinical Research Infrastructures Network (ECRIN)[59] both of which form part of the infrastructure needed to enable health applications of nanotechnology.

Other mechanisms to support research and innovation in nanotechnology and health are outlined in the section on Other EU Policies: Industry, later in this chapter. They include:

- EUREKA's Eurostars;
- European Technology Platforms; and
- Joint Technology Initiatives (and Joint Undertakings).

The next section reports on funding and participation data for the Sixth and Seventh EU Framework Programmes, FP6 and FP7.

[58] http://ec.europa.eu/programmes/horizon2020/en/news/biospecimens-beyond-borders
[59] http://ec.europa.eu/programmes/horizon2020/en/news/creating-single-european-area-clinical-research

4.2 The EU Framework Programme: funding and participation data for FP6 and FP7[60]

4.2.1 Overview

Project-related data was extracted from the eCorda database for the EU Sixth Framework Programme (FP6) and the EU Seventh Framework Programme (FP7)[61]. The total number of projects was 35,265, of which 25,238 were FP7 projects and 10,027 were FP6 projects. There were 210,177 participations, of which 133,615 were in FP7 and 76,562 were in FP6.

From the initial set of 35,265 projects, 3,544 were found to be related to nanotechnology in that they contained the term "nano"[62] in the title or abstract of the project. Thus, nanotechnology projects form approximately 10% of the total FP projects. The share of nanotechnology projects increased slightly between FP6 (9.1%) and FP7 (10.4%).

74% of the 3,544 projects were FP7 projects and 26% were FP6 projects. The relative shares of nanotechnology projects were similar to those found for FP projects in general (72% in FP7 and 28% in FP6).

Table 4-1: Number of projects and shares for total projects and for nanotechnology

		Total	FP7	FP6
FP total	Number of FP projects	35,265	25,238	10,027
	Share of FP projects (total)	100%	71.6%	28.4%
Nanotechnology	Number of FP projects	3,544	2,636	908
	Share of FP projects (NT)	100%	74.4%	25.6%
Share of nanotechnology of total FP (projects)		10.0%	10.4%	9.1%

Number and share of health nanotechnology projects

The number of projects (in FP6 and FP7 together) that were related to both health and nanotechnology was determined, using a keyword search[63], to be 944, approximately 27% of the total number of projects related to nanotechnology. The percentage of health nanotechnology projects was higher in FP7 at the time of extraction of the data (28%) than it was in FP6 (22%), indicating that the relevance of health has increased within nanotechnology FP-activities from FP6 to FP7.

[60] As some projects make reference to more than one of the health sub-sectors, there has been a simple allocation made. Where two sub-sectors are mentioned, half a project is given to each sub-sector. Where three are mentioned, a third of a project is allocated to each. This method can result in under and over estimates of projects e.g. where one third of a project (0.3333 recurring) is rounded down to 0.3 or two thirds (0.66666 recurring) are rounded up to 0.7. There are therefore some small rounding errors in the tables and charts.

[61] It should be noted that the FP7 projects may not represent the total number of projects that will take place during FP7 but include only the projects funded up until the date when the extraction of data from eCorda was made (January 2015).

[62] The term "nano" could appear as a part of a word (e.g. nanotechnology, nanoscience, nanomaterial, nanoscale), as a part of compound word separated with hyphen (e.g. nano-science) or as an independent word "nano".

[63] See Annex for details

Table 4-2: Number of projects and shares for nanotechnology and for nanotechnology and health

	Numbers of Projects		
	Total	FP7	FP6
Total FP projects, all topics	35,265	25,238	10,027
Nanotechnology FP projects	3,544	2,636	908
Health nanotechnology FP projects	944	745	199
	Shares (number of projects)		
	Total	FP7	FP6
Total FP Projects, all topics	100%	71.6%	28.4%
Nanotechnology (NT) FP projects	100%	74.4%	25.6%
Health NT projects as % of all NT projects	26.6%	28.3%	21.9%
Health NT as % of all FP	2.7%	3.0%	2.0%

FP7 participations make up 64% of total participations and FP6 participations make up 36%. For nanotechnology participations, FP7 make up 65% and FP6 35%, very similar to the overall FP participation percentages. Looking at health nanotechnology as a proportion of overall nanotechnology, in FP7 27% of participations related to health while in FP6 the health percentage of nanotechnology was 24%.

Funding of health nanotechnology projects

Project funding for health nanotechnology (NT) from the EU budget more than tripled from FP6 (EUR 415M out of a total of EUR 1,703M) to FP7 (EUR 1,339M out of a total of EUR 4,661M). In terms of funding, this indicates that the relative importance of health NT activities increased from 24% in FP6 to 29% in FP7. Thus the health NT EC funding has increased in both absolute and relative terms, as shown in the figure below.

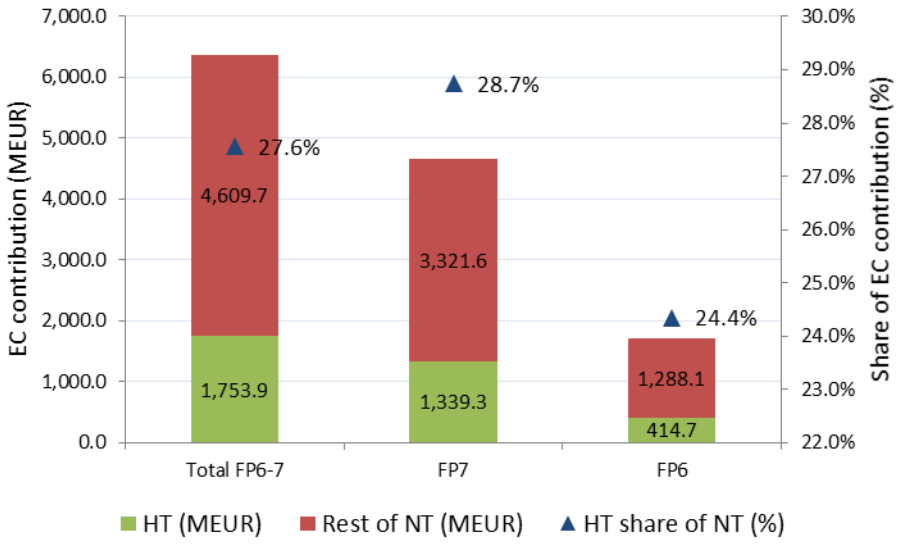


Figure 4-1: Funding of health nanotechnology for FP6 and FP7 together, for FP7 and for FP6

Participant type in health nanotechnology projects

Participation in FP6 and FP7 for health nanotechnology was similar across the two Programmes, as seen in the figure below. The higher education sector (HES) was responsible for over half of

participations (as measured by funding) with other research organisations (REC) at between approximately 22% and 27%. Companies have so far been more engaged in FP7 than they were in FP6 mainly due to increased participation by SMEs (large companies (PCO) having 6% of funding from participations in both but SMEs growing from 9% to 16%). It is worth considering that some of this effect may be due to re-categorisation as the percentage of organisations identified as "Other" has dropped from 8% to 1% of funding.

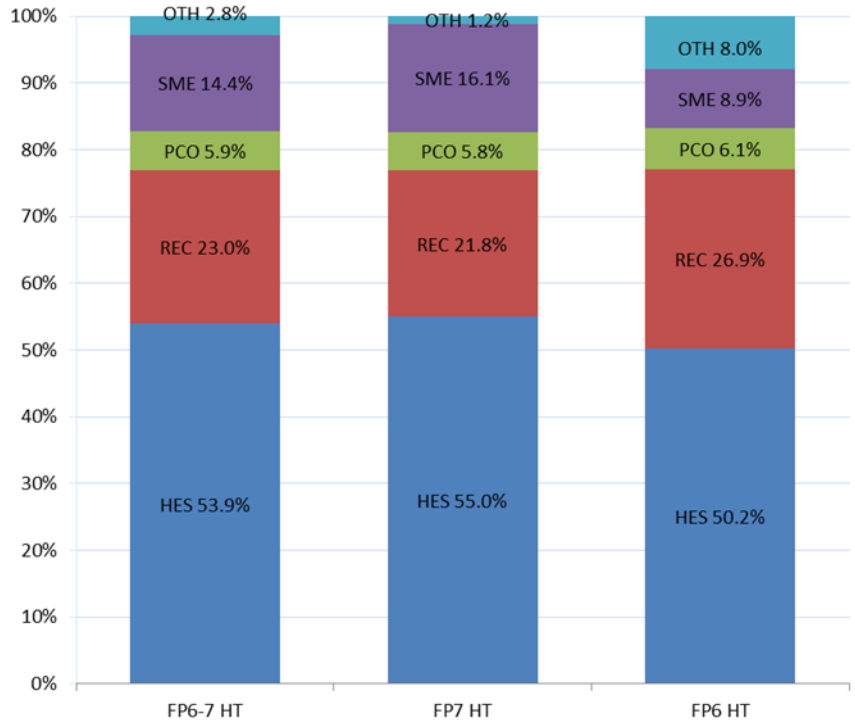


Figure 4-2: Shares of EC contribution by organisation type for nanotechnology and health

4.2.2 Activities by programme and sub-programme

4.2.2.1 FP6 health nanotechnology activities

Nanotechnology health projects made up approximately 2% of the total number of projects in FP6 and, with 199 health NT projects, over 20% of FP6 NT projects.

FP6 was structured in three main blocks of activities:

1) Focusing and integrating the ERA - divided into *Thematic Priorities* and *Specific Activities*;
2) Structuring the ERA – including research and innovation, research mobility, infrastructure development and science and society; and
3) Strengthening the ERA – for co-ordination and policy activities.

There was, in addition, the EURATOM activity.

Table 4-3: FP6 health nanotechnology activities by programme and sub-programme

FP6 Summary	Number of projects			EC funding (MEUR)			Share of EC funding (%)		
	FP6 Total	NT	HT	FP6 Total	NT	HT	FP6	FP6 NT	FP6 HT
I Focusing and Integrating ERA	**4,735**	**455**	**120**	**13,445.0**	**1,383.6**	352.0	80.5%	81.3%	84.9%
Thematic Priorities	3,374	389	101	12,027.5	1,314.8	327.2	72.1%	77.2%	78.9%
1. Life Sciences	602	20	20	2,336.5	54.1	54.1	14.0%	3.2%	13.1%
2. Information Society	1,089	80	12	3,798.9	346.1	62.1	22.8%	20.3%	15.0%
3. NMP	444	271	68	1,534.2	870.1	210.1	9.2%	51.1%	50.7%
4. Aeronautics and Space	241	5	0	1,066.1	11.6	0	6.4%	0.7%	0.0%
5. Food Quality and Safety	189	0	0	754.2	0	0	4.5%	0.0%	0.0%
6. Sustainable Development	666	10	0	2,300.9	30.5	0	13.8%	1.8%	0.0%
7. Citizens and Governance	143	3	1	236.6	2.4	0.8	1.4%	0.1%	0.2%
Specific Activities	1,361	66	19	1,417.5	68.8	24.8	8.5%	4.0%	6.0%
Policy Support	520	29	12	604.2	40.7	19.4	3.6%	2.4%	4.7%
Horizontal Research Involving SMEs	490	29	6	463.1	24.7	5.1	2.8%	1.4%	1.2%
International co-Operation	351	8	1	350.3	3.4	0.3	2.1%	0.2%	0.1%
II Structuring ERA	**5,096**	**449**	**79**	**2,744.2**	**303.1**	62.7	16.4%	17.8%	15.1%
Research and Innovation	240	3	1	224.0	3.9	0.9	1.3%	0.2%	0.2%
Human Resources and Mobility	4,546	420	72	1,723.1	219.2	47.2	10.3%	12.9%	11.4%
Research Infrastructures	147	17	3	717.6	74.3	11.6	4.3%	4.4%	2.8%
Science and Society	163	9	3	79.5	5.8	3.1	0.5%	0.3%	0.7%
III Strengthening ERA	118	3	0	317.3	8.0	0	1.9%	0.5%	0.0%
Co-ordination of Activities	99	3	0	303.8	8.0	0	1.8%	0.5%	0.0%
Research & Innovation Policies	19	0	0	13.5	0	0	0.1%	0.0%	0.0%
EURATOM	78	1	0	185.7	8.0	0	1.1%	0.5%	0.0%
TOTAL	10,027	908	199	16,692.2	1,702.8	414.7	100.0%	100.0%	100.0%

In FP6, activities specific to nanotechnology and health made up approximately 24% of all nanotechnology activities as measured by EC funding allocation. They took place mainly under the two priorities of (i) Focusing and integrating the ERA and (ii) Structuring the ERA.

Within the Thematic Priorities of the former:

- NMP (Nanotechnologies and nanosciences, knowledge based multi-functional materials and new production processes and devices) had the largest number of health nanotechnology projects (68) and a total of EUR 210 million of EC funding (over 50% of total health nanotechnology funding);
- Information Society Technologies (IST) had 12 projects and EUR 62 million of EC funding (15% of total); and

- Life sciences had 20 projects with EUR 54 million (13% of total).

These three Thematic Priorities together were therefore the recipients of almost 80% of the funding for health nanotechnology in FP6.

Within the priority of Structuring the ERA, 72 projects for Human Resources and Mobility received EUR 47M (11% of total health nanotechnology EC funding, 36% of projects).

4.2.2.2 FP7 health nanotechnology activities

Health nanotechnology projects comprised approximately 3% of the total number of projects in FP7 and, with 745 health nanotechnology projects, 28% of FP7 nanotechnology projects[64]. Nanotechnology activities make up approximately 10% of the total EC FP7 funding to date, and health nanotechnology activities about 29% of nanotechnology funding and 3% of total FP7 funding.

The broad objectives of FP7 group into four categories:
- Co-operation;
- Ideas;
- People; and
- Capacities.

The largest amount of funding for health nanotechnology is seen under the Co-operation Specific Programme NMP (for Nanosciences, nanotechnologies, Materials and new Production technologies) with EUR 486M (36% of health nanotechnology funding). In terms of numbers of projects, NMP has 15% of health nanotechnology projects (114 out of 745).

European Research Council (Ideas) activities have the next highest funding with EUR 280M (21% of health nanotechnology funding) and 162 projects (22% of projects), followed by Marie Curie Actions (People) with EUR 186M (14%) of health nanotechnology funding and 354 projects (48%). Compared with FP6, the relative importance of activities for Human Resources and Mobility has increased in both numbers of projects (from 72 to 354, 36% to 48% of projects) and funding (from EUR 47M to EUR 186M, 11% to 14% of health nanotechnology funding).

The themes of ICT and health are strong areas for FP7 health nanotechnology projects and EC funding specifically:

- For Health, 33 projects (4%) with EUR 157M (12% of health nanotechnology EC funding); and
- For ICT, 26 projects (3%) with almost EUR 108M (8% of health nanotechnology EC funding).

Thus, the three Co-operation actions of NMP, Health and ICT have, to date, 56% of health nanotechnology funding. Together with ERC and Marie Curie Actions, these five activities have over 90% of total health nanotechnology EC funding.

[64] Data extracted January 2015

Table 4-4: FP7 health nanotechnology activities by programme and sub-programme

FP7 Summary	Number of projects			EC funding (MEUR)			Share of EC funding (%)		
	Total FP7	FP7 NT	FP7 HT	Total FP7	FP7 NT	FP7 HT	FP7	FP7 NT	FP7 HT
CO-OPERATION	**7,834**	**756**	**192**	**28,336.3**	**2,803.8**	**820.0**	**63.1%**	**60.2%**	**61.2%**
Health	1,008	33	33	4,791.7	157.0	157.0	10.7%	3.4%	11.7%
Food, Agri and Bio	516	25	12	1,850.7	97.1	45.9	4.1%	2.1%	3.4%
ICT	2,328	175	26	7,877.0	561.3	107.5	17.5%	12.0%	8.0%
NMP	805	412	114	3,238.6	1,595.6	486.0	7.2%	34.2%	36.3%
Energy	368	24	1	1,707.4	81.5	3.0	3.8%	1.7%	0.2%
Environment	494	10	0	1,719.3	26.9	0.0	3.8%	0.6%	0.0%
Transport	719	12	0	2,284.2	61.5	0.0	5.1%	1.3%	0.0%
Socio-Economic Sciences	253	0	0	579.6	0.0	0.0	1.3%	0.0%	0.0%
Space	267	14	0	713.3	31.7	0.0	1.6%	0.7%	0.0%
Security	314	5	1	1,295.5	14.1	3.4	2.9%	0.3%	0.3%
General Activities	26	0	0	312.7	0.0	0.0	0.7%	0.0%	0.0%
Joint Technology Initiatives	736	46	5	1,966.4	177.0	17.1	4.4%	3.8%	1.3%
IDEAS	**4,525**	**572**	**162**	**7,673.5**	**1,026.1**	**280.4**	**17.1%**	**22.0%**	**20.9%**
European Research Council	4,525	572	162	7,673.5	1,026.1	280.4	17.1%	22.0%	20.9%
PEOPLE	**10,716**	**1,158**	**354**	**4,777.5**	**579.9**	**186.2**	**10.6%**	**12.4%**	**13.9%**
Marie-Curie Actions	10,716	1,158	354	4,777.5	579.9	186.2	10.6%	12.4%	13.9%
CAPACITIES	**2,025**	**149**	**37**	**3,772.0**	**249.9**	**52.7**	**8.4%**	**5.4%**	**3.9%**
Research Infrastructures	341	18	2	1,528.4	72.2	8.6	3.4%	1.5%	0.6%
Research for the benefit of SMEs	1,028	70	23	1,249.1	86.1	25.9	2.8%	1.8%	1.9%
Regions of Knowledge	84	4	1	126.7	7.3	2.6	0.3%	0.2%	0.2%
Research Potential	206	27	6	377.7	55.1	12.5	0.8%	1.2%	0.9%
Science in Society	183	16	3	288.4	16.5	2.2	0.6%	0.4%	0.2%
Research policies	26	0	0	28.3	0.0	0.0	0.1%	0.0%	0.0%
International Co-operation	157	14	2	173.4	12.7	0.9	0.4%	0.3%	0.1%
EURATOM	138	1	0	358.1	1.1	0.0	0.8%	0.0%	0.0%
Fusion	4	0	0	5.2	0.0	0.0	0.0%	0.0%	0.0%
Fission	134	1	0	352.8	1.1	0.0	0.8%	0.0%	0.0%
TOTAL	**25,238**	**2,636**	**745**	**44,917.3**	**4,660.8**	**1,339.3**	**100.0%**	**100.0%**	**100.0%**

4.2.3 Activities by participant type

The table below shows the participations in FP6 and FP7 for the Higher Education Sector (HES), other research organisations (RECs), large companies (PCO), SMEs and other organisations. As well as the number of participations (Particip.), the table shows the total EC funding and share of funding for each, for all FP6 and FP7 and for NT and health NT.

Table 4-5: Participations in FP6 and FP7 including funding and share of funding[65]

	Total FP6 and FP7			NT in FP6 and FP7			Health in NT in FP6 and FP7		
	Particip.	EC Funding	Share of Funding	Particip.	EC Funding	Share of Funding	Particip.	EC Funding	Share of Funding
HES	76,777	25,736.0	41.8%	7,671	3,019.5	47.5%	2,120	943.9	53.9%
REC	53,384	17,304.4	28.1%	4,696	1,778.1	28.0%	1,089	402.8	23.0%
PCO	25,067	7,021.3	11.4%	2,275	615.4	9.7%	395	102.7	5.9%
SME	29,428	6,882.6	11.2%	3,239	769.1	12.1%	960	252.8	14.4%
Other	24,961	4,626.8	7.5%	1,059	174.2	2.7%	277	48.6	2.8%
Total	**209,617**	**61,571.1**	**100.0%**	**18,940**	**6,356.2**	**100.0%**	**4,841**	**1,750.9**	**100.0%**

Organisations in the higher education sector receive 54% of FP health nanotechnology funding. The figure for nanotechnology is lower at 48% and for FP overall it is lower still at 42%. This result matches with expectations as much of health research takes place in the higher education sector (including universities and hospitals).

Research organisations (REC) receive a smaller share of funding (23%) for health nanotechnology than in nanotechnology in general (28%) or in FP overall (28%) indicating that health research is less important for research performers that are not in the higher education sector.

The participation of companies is low for health nanotechnology research in the FPs at 6% for large companies but high for SMEs at 14%. Large companies have 11% participation in FP overall and 10% for nanotechnology FP research. SMEs are more active in health nanotechnology research than in nanotechnology FP research (12%) or FP research overall (11%). This finding may reflect the dynamism of the health research sector, many small companies being created from the research base (as university start-ups or industry spin-outs, undertaking research and development activity for a relatively short while and then being integrated into larger enterprises (acquisitions and mergers).

4.2.4 Activity by organisations receiving funding

The largest amounts of funding for health nanotechnology activities have been received by the CNRS (Centre National de la Recherche Scientifique)[66] in France, participating in 83 health nanotechnology projects and receiving funding of EUR 32M. The Max Planck Gesellschaft from Germany is in the second position with 51 projects and EUR 29M. The third most active is Ecole Polytechnique Federale de Lausanne (EPFL), Switzerland (48 projects and EUR 28M).

All top ten recipients are research organisations and/ or from the higher education sector. The only organisation in the top 25 that falls outside of those categories is Philips Electronics Nederland P.V., ranked 18. The top ten organisations are from France, Germany, Switzerland, UK, Spain, Sweden and Denmark.

[65] The EC contribution in eCorda project and participant database differ by a small amount. The figures reported here for participants therefore do not exactly match those for projects in previous sections.

[66] Researchers associated with the CNRS may be located within any of its ten research organisations throughout France.

Table 4-6: Organisations participating in FP6 and FP7, top 25 ranked by funding received

	Health: Top participants	Country	No. of Projects	EC Funding (MEUR)	Share of HT Funding
1	Centre National de la Recherche Scientifique (CNRS)	FR	83	32.4	1.85%
2	Max Planck Gesellschaft	DE	51	28.9	1.65%
3	Ecole Polytechnique Federale de Lausanne (EPFL)	CH	48	27.8	1.59%
4	Fraunhofer-Gesellschaft	DE	46	25.2	1.44%
5	Commissariat à l'Energie Atomique et aux Energies Alternatives (CEA)	FR	38	21.8	1.24%
6	Eidgenoessische Technische Hochschule Zuerich (ETHZ)	CH	26	20.8	1.19%
7	Imperial College of Science, Technology and Medicine	UK	38	19.4	1.11%
8	Agencia Estatal Consejo Superior de Investigaciones Científicas (CSIC)	ES	38	16.0	0.92%
9	Karolinska Institutet	SE	21	15.9	0.91%
10	Danmarks Tekniske Universitet	DK	30	15.0	0.86%
11	Kungliga Tekniska Hoegskolan (KTH)	SE	25	14.8	0.85%
12	Universiteit Twente	NL	25	14.1	0.80%
13	Consiglio Nazionale delle Ricerche	IT	41	13.6	0.78%
14	Tel Aviv University	IL	26	12.9	0.74%
15	Universitaet Ulm	DE	5	12.3	0.70%
16	Universiteit Utrecht	NL	18	12.2	0.70%
17	University of Oxford	UK	24	11.2	0.64%
18	Philips Electronics Nederland B.V.	NL	15	11.0	0.63%
19	University of Leeds	UK	15	10.1	0.58%
20	Technion Israel Institute of Technology	IL	16	10.1	0.58%
21	Stichting Katholieke Universiteit	NL	14	10.0	0.57%
22	University College Dublin (UCD)	IE	18	9.8	0.56%
23	Universiteit Gent	BE	15	9.7	0.55%
24	Katholieke Universiteit Leuven	BE	15	9.6	0.55%
25	Lunds Universitet	SE	21	9.3	0.53%

The table below indicates the most active companies in FP health nanotechnology projects by funding, the majority being SMEs (17 out of the 25, 6 out of the top 10).

Table 4-7: Companies participating in FP6 and FP7, top 25 ranked by funding received

	Health - Top Company Participants	Country	SME	No. of Projects FP6-7	EC Funding (MEUR)
1	Philips Electronics Nederland B.V.	NL		15	10.97
2	Laboratoire Biodim	FR	SME	1	3.91
3	Microfluidic Chipshop GmbH	DE	SME	8	3.22
4	QuantuMDx Group Limited	UK	SME	1	2.63
5	Philips Technologie GmbH	DE		5	2.19
6	MBN Nanomaterialia Spa	IT	SME	4	1.83
7	Fluigent SA	FR	SME	3	1.79
8	Nanocyl SA	BE	SME	7	1.65
9	Avanticell Science Ltd	UK	SME	4	1.64
10	Procarta Biosystems Limited	UK	SME	2	1.55
11	Solae Denmark AS	DK		2	1.54
12	Osm-Dan Ltd.	IL	SME	9	1.51
13	Luxcel Biosciences Ltd.	IE	SME	3	1.50
14	IBM Research GmbH	CH		2	1.49
15	Nanopet Pharma GmbH	DE	SME	3	1.49
16	Sanofi-Aventis Recherche & Developpement	FR		4	1.47
17	Explora Srl	IT	SME	2	1.47
18	The Bio Nano Centre Ltd.	UK	SME	2	1.46
19	Nanovector Srl	IT	SME	4	1.43
20	Agilent Technologies Osterreich GmbH	AT		4	1.40
21	Robert Bosch GmbH	DE		2	1.37
22	Imasonic Sas	FR	SME	2	1.36
23	M-Squared Laser Ltd.	UK	SME	3	1.36
24	Diagnoswiss SA	CH	SME	4	1.33
25	Cellectis AB	SE	SME	1	1.32

Philips Electronics (the Netherlands), as the company that is the most active in terms of funding, is followed by two SMEs, Laboratoire Biodim (France) and Microfluidic ChipShop GmbH (Germany). Company participation is also rather spread among different actors as only one company, Philips Electronics, participated in more than ten projects during FP6 and FP7 and only four in total participated in more than five projects, three of them being SMEs.

4.2.5 Participation by country

In total, 58 countries took part in health nanotechnology projects funded under FP6 and FP7. The top five countries received over half of the total funding: Germany (18%), the UK (14%), France (9%), Italy (8%) and the Netherlands (7%). The top fifteen countries (with over 90% of the health nanotechnology funding) are shown in the table below.

Table 4-8: Top fifteen countries for FP participation ranked by funding received

Rank	Country	Health NT Funding (MEUR)	% of Funding
1	DE	314.5	18.0
2	UK	251.6	14.4
3	FR	161.1	9.2
4	IT	130.8	7.5
5	NL	119.9	6.8
6	ES	119.1	6.8
7	CH	109.5	6.3
8	SE	87.8	5.0
9	BE	65.3	3.7
10	IL	64.3	3.7
11	IE	42.5	2.4
12	DK	42.5	2.4
13	AT	40.0	2.3
14	FI	35.2	2.0
15	GR[67]	30.9	1.8
	TOTAL	1,615	92%

Comparison can be made with the data for the country of origin of the participants for both nanotechnology funding and for FP funding overall. In the table below, the data is ordered by the ranking for health nanotechnology funding received by the country. The same five countries are at the top of the ranking in terms of their share of funding for FP overall. Germany, the UK, France, Italy and the Netherlands are the top five most active countries for participation in both FP activities and health nanotechnology activities measured as country share of total funding. In all cases (FP, nanotechnology and health nanotechnology), the top ten countries take approximately 80% of funding.

[67] Greece, also indicated by EL. This document uses ISO 2-letter codes with Greece designated as GR.

Table 4-9: Country ranking by FP funding for top ten in FP, nanotechnology and health nanotechnology

(Listed in order of received health nanotechnology funding, highest at the top of the table)

	FP total			Nanotechnology			Health Nanotechnology		
	MEUR	Rank	Share of FP	MEUR	Rank	Share of NT	MEUR	Rank	Share of Health NT
DE	10,164.10	1	16.50%	1,121.50	1	17.60%	314.50	1	18.00%
UK	9,295.20	2	15.10%	845.90	2	13.30%	251.60	2	14.40%
FR	7,319.30	3	11.90%	760.90	3	12.00%	161.10	3	9.20%
IT	5,046.50	4	8.20%	505.20	4	7.90%	130.80	4	7.50%
NL	4,438.40	5	7.20%	444.30	6	7.00%	119.90	5	6.80%
ES	4,200.60	6	6.80%	481.00	5	7.60%	119.10	6	6.80%
CH	2,503.20	8	4.10%	338.00	7	5.30%	109.50	7	6.30%
SE	2,386.70	9	3.90%	271.60	8	4.30%	87.80	8	5.00%
BE	2,518.00	7	4.10%	258.40	9	4.10%	65.30	9	3.70%
IL	1,055.00	14	1.70%	142.70	13	2.20%	64.30	10	3.70%
TOTAL	48,927		79.5%	5,170		81.3%	1424		81.3%[68]

As shown in the figure below, participants from Germany, Switzerland, Sweden and Israel are more active in health nanotechnology projects than in FP activities in general and more active in nanotechnology than in FP overall.

France, Italy, the Netherlands and Belgium participate less actively in health nanotechnology when compared to their participation in the FPs as whole. The United Kingdom has higher participation in health nanotechnology than in nanotechnology but its health nanotechnology participation is lower than its overall FP participation.

[68] As some projects make reference to more than one of the health sub-sectors, there has been a simple allocation made. Where two sub-sectors are mentioned, half a project is given to each sub-sector. Where three are mentioned, a third of a project is allocated to each. This method can result in under and over estimates of projects e.g. where one third of a project (0.3333 recurring) is rounded down to 0.3 or two thirds (0.66666 recurring) are rounded up to 0.7. There are therefore some small rounding errors in the tables and charts.

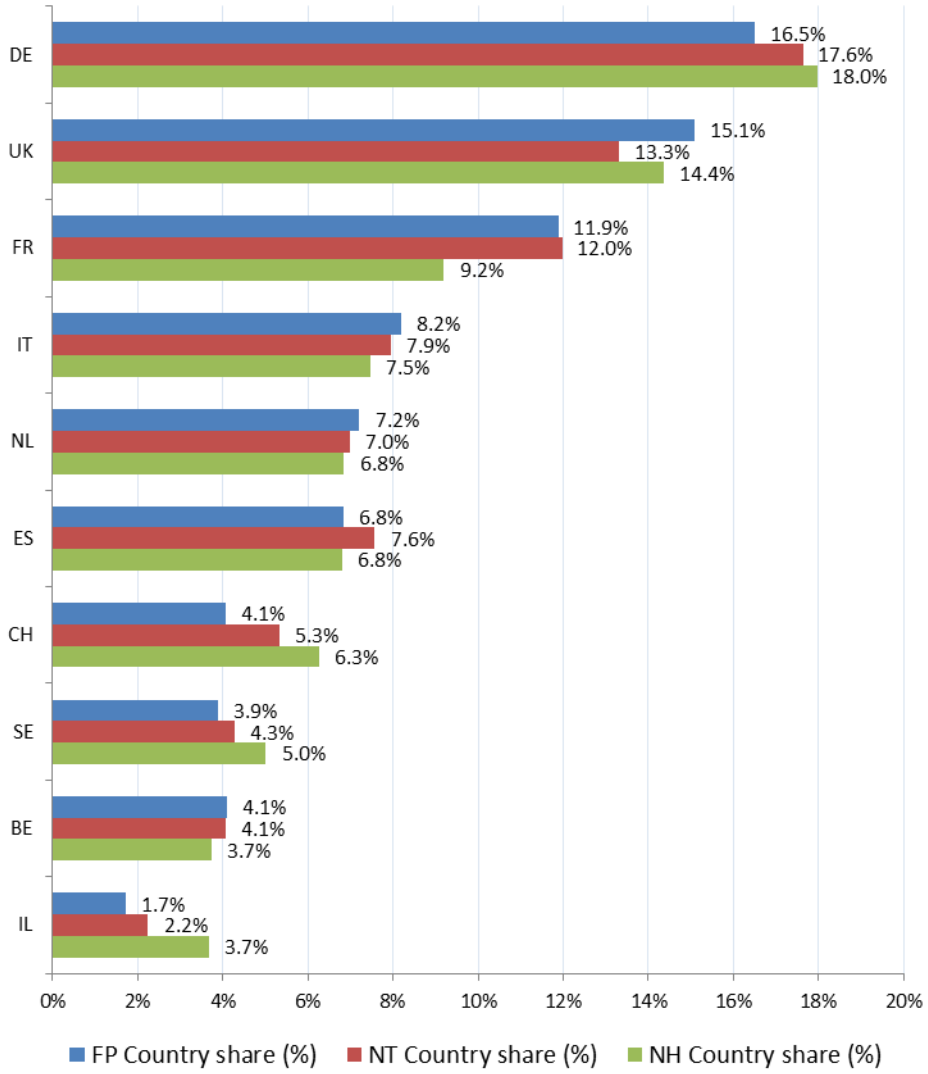


Figure 4-3: Percentage shares of FP funding by country in FP, nanotechnology and health nanotechnology

The figure below indicates the EC funding for health nanotechnology activities in FP6 and FP7 in terms of MEUR (bars, use left axis) and country shares (dots, use right axis) for the ten countries receiving the most funding. The funding received by Germany decreased from FP6 to FP7[69] with 21 % of the funding for health nanotechnology activities in FP6 whereas in the FP7 the country share of funding was 17%. Similarly, for France and the Netherlands the country share of funding decreased between FP6 and FP7. This may indicate that although these countries are still among the largest receivers of funding in FPs, the other countries seem to be catching up. The EU28 countries that have received relatively more funding so far in FP7 than in FP6 are the UK (12 % in FP6 and 15 % in FP7) and Spain (5% in FP6 and 7% in FP7). For the rest of the EU28 countries, the funding shares remained rather unchanged between FP6 and FP7.

[69] Data downloaded in January 2015.

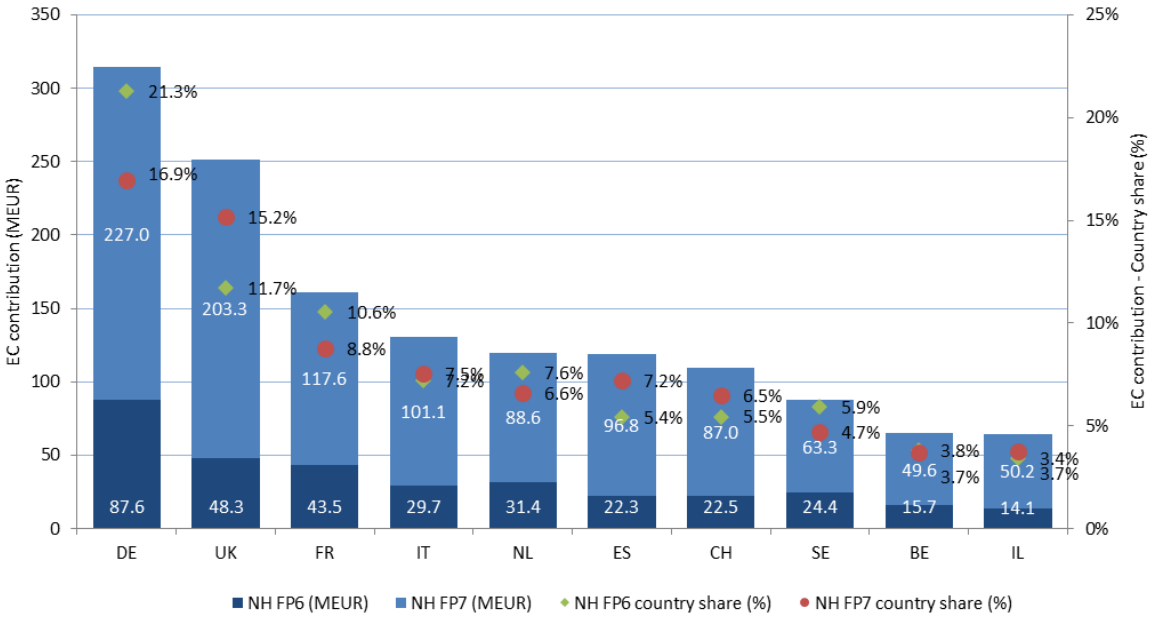


Figure 4-4: EC funding for health nanotechnology activities in FP6 and FP7 in MEUR and country shares

4.2.6 Health nanotechnology sub-sectors in FP6 and FP7

The five health sub-sectors under consideration in this report are cancer treatment, cardiovascular disease, diabetes, infectious diseases and neurodegenerative diseases (NDG). These make up over 40% of activity in FP6 and FP7, many of the other activities[70] being of a generic nature of value in the prevention, diagnosis or treatment of multiple diseases or related to topics not under consideration (e.g. hospital equipment, prostheses, etc.) except in so far as they are relevant to the five sub-sectors.

The figures show the number of projects and share of funding for the health nanotechnology sub-sectors, with cancer predominating, followed by infectious diseases and cardiovascular disease.

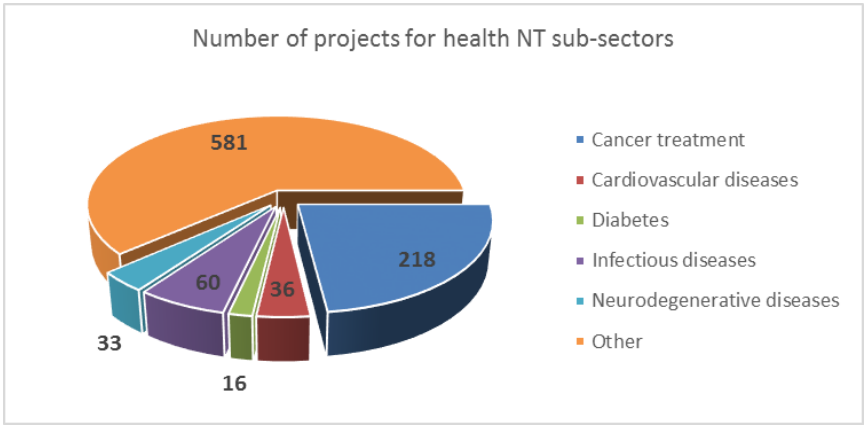


Figure 4-5: Number of projects in FP6 and FP7 for health nanotechnology by sub-sector

[70] "Other" includes a wide variety of projects, for example those related to general health research involving nanotechnology but not directly applied to any of the diseases areas analysed as sub-sectors within this document. These projects include topics such as research related to molecular biology with health application (genetics, DNA, stem cells etc.) and research activities related to diagnostics and imaging not directly applied to any of the above mentioned disease categories.

For neurodegenerative diseases, the projects numbers are similar to cardiovascular diseases but the funding is much less.

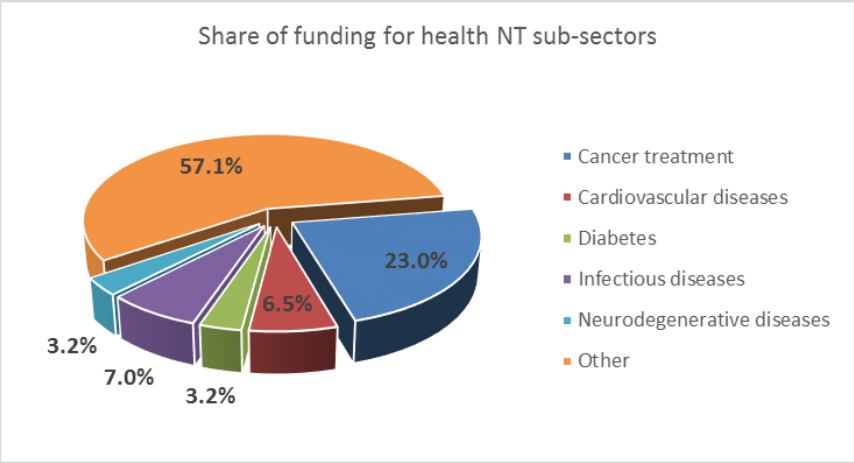


Figure 4-6: Share of EC funding for health nanotechnology sub-sectors

Each of the sub-sectors is considered in more detail in separate landscape reports of the NanoData project. The main messages from those reports are:

- The most typical funding instrument is the collaborative RTD actions, being as high as 92% of the funding in cardiovascular disease.
- Cancer treatment and neurodegenerative diseases are more typical topics for research actions of the ERC than the rest of the sub-sectors.
- The projects focused on infectious diseases and diabetes receive more funding through actions supporting adoption and innovation, although the share of funding allocated through these instruments is rather modest (6% each in infectious diseases and diabetes).
- In FP projects focused on neurodegenerative diseases, higher education institutes receive 67 % of the total funding of the sub-sector. This is higher than in the rest of the sub-sectors, in which the higher education receives roughly 50 % of the funding.
- The projects dedicated to neurodegenerative diseases have less participation from the company sector (13% large companies and SMEs together) than those from other sub-sectors and an especially low share of funding going to large companies (1.4%).
- SMEs receive a proportionally higher share of the sub-sector funding in infectious diseases (26%) and diabetes (19%) when compared to other sub-sectors. This finding is aligned with these sectors receiving more funding for innovation actions.
- Germany, the UK and France are the top three countries receiving funding in all sub-sectors. For cancer treatment and cardiovascular disease, these three countries together receive 40 % of the funding, while in neurodegenerative diseases they receive over 50%.
- The non-classified health nanotechnology activities include less collaborative RTD actions than the rest of the sub-sectors and in turn receive more funding allocated through research support actions like knowledge transfer or support to policymaking. This confirms the general nature of the non-classified health nanotechnology activities in the category "Other".

4.2.7 Snapshot of outputs from FP7

A review was undertaken of 106 FP7 nanotechnology projects reported on via the SESAM system in which participants report themselves on their project. The projects are random, being the first ones to report, which they can only do when the project has finished. In addition, the information has not been normalised to take into account the type and size of project. It is therefore not intended here to present the information as a rigorous review, only as a snapshot at a point in time of FP7 projects that have reported to date.

In the review of the 106 SESAM reports, it was found that:

- 82% of projects had published work during the project, the total number of publications being 1783 and the average number being almost 17; and
- 32% of projects had applied for patents, a total of 73 patents having been applied for, an average

of 0.7 per project. Of these, 18 have been applied for at the European Patent Office, 20 under the PCT at WIPO, 6 at the USPTO and 30 at other (national) patent offices.

Of the 106 projects, 27 were classified by review as being related to health nanotechnology. Those 27 projects reported outputs of:

- 664 publications, an average of 24 publications per project, higher than for nanotechnology overall; and
- 29 patent applications, an average of more than one per project, higher than for nanotechnology overall.

Thus, of the projects under review, health nanotechnology projects under FP7 produce more than the average number of publications and patents for nanotechnology.

The next section considers EU policies and programmes that complement the supports for nanotechnology and health described previously in this section for the EU Framework Programmes.

4.3 Other EU policies and programmes

4.3.1 EU policies and programmes: Industry

Policies related to industry and economic development fall under the Framework Programmes (e.g. for ICT) and other EU measures (e.g. under the remit of DG Enterprise and Industry). Some, addressing environmental health and safety, are identified below.

ICT funding has direct relevance to some health activities. Under FP7, the objective of ICT research funding is to strengthen the science and technology base to the level of global leadership, to stimulate innovation and creativity in products, processes and services, and to enhance the use of ICT for public benefit in society and the economy. EUR 9.1 million have been allocated to this theme under FP7, making this the largest in budgetary terms under the Co-operation Programme.

> ***ICT, Nano and Health: The Micro- and Nano-Bio Systems cluster in FP6 and FP7[71]***
>
> One ICT activity of relevance to nanotechnology and health is the Micro- and Nano-Bio Systems cluster that looks at how systems can be integrated for applications that have, or interact with, biological components. Other areas of application include environmental monitoring, and food and beverage quality and safety.
>
> MNBS projects to date have had targets of achieving substantial improvements via system integration (e.g. miniaturisation and reduced power consumption, integration of molecular and cell biology), improving system quality and/or reliability, and reducing the time-to-market. MNBS has sub-groups on biomedical applications; miniaturised and lab-on-chip systems for biological (in vitro), chemical and biochemical analysis; and systems for in vivo interaction with the human body, etc. These aim, *inter alia*, to accelerate the development of integrated diagnostic, monitoring and therapeutic devices.

Research by companies in the EU is also supported through the EUREKA Eurostars[72] initiative established under Article 185 of the Treaty on the Functioning of the European Union (TFEU), in partnership between the European Commission, the Member States and the countries associated with the Framework Programmes. Eurostars supports European R&D performing SMEs to commercialise their research. It helps them to accelerate the time to market of products, processes and services to the market. It also encourages them to develop and internationalise their business. Funding of up to EUR 100 million was made available through EUREKA for the period 2008-2013, the EU contribution comprising a maximum of one third of the funding provided by the participating countries. Funding for Eurostars has continued with a total public budget of EUR 1.14 billion in 2014-2020, EUR 861 million of national funding and EUR 287 million of EU funding from Horizon 2020. In the 39 success stories identified for Eurostars, two relate to nanotechnology and many to health, including medical devices and genetic profiling.

Another type of mechanism is the European Technology Platform (ETP) including the ETP Nanomedicine (ETPN)[73]. ETPs are bottom-up, industry-led stakeholder fora, the aim of which is to increase interaction between research actors and to facilitate the development of medium to long-term research and technological goals and associated roadmaps. They do not fund research projects but are a co-ordination mechanism. ETPs now exist across the themes of energy, environment, ICT, production and processes, transport and the bio-based economy. The ETPN sits under the theme of Production and Processes. There are three ETPN stakeholder priority areas: nanotechnology-based diagnostics including imaging; targeted drug delivery and release; and regenerative medicine. Currently, the ETP has 120 member organisations of which four are hospitals, six are industrial enterprises and 16 are SMEs, the remaining 94 being research bodies. Members pay an annual fee of between EUR 5,000 for large industry and EUR 500 for research organisations.

Another ETP of relevance to health is EPoSS[74], the ETP for smart systems integration and integrated

[71] http://cordis.europa.eu/fp7/ict/micro-nanosystems/home_en.html
[72] https://www.eurostars-eureka.eu/
[73] http://www.etp-nanomedicine.eu/
[74] http://www.smart-systems-integration.org/public

micro- and nanosystems. EPoSS represents the Smart Systems community in the Joint Technology Initiative for Electronic Components and Systems for European Leadership (JTI ECSEL). The platform aims to provide a common European approach on innovative and smart systems integration from research to production, with an agreed roadmap for action and a strategic R&D agenda and to provide the resources to deliver the roadmap from public and private sources. EPoSS has members in over 20 Member States including large companies, SMEs, universities and other public organisations undertaking research and development.

Joint Technology Initiatives (JTIs) are long-term Public-Private Partnerships which are managed within dedicated structures based on Article 187 of the Treaty on the Functioning of the European Union (TFEU). JTIs support large-scale multinational research activities in areas of major interest to European industrial competitiveness, as well as issues of high societal relevance. They are established on the basis of European Technology Platforms (ETPs) in those cases where the scale and scope of the initiative make loose co-ordination through ETPs and support by the regular instruments of the Framework Programme for Research and Development insufficient[75]. Six areas were identified for the development of a JTI: Innovative Medicines; Nanoelectronics (ENIAC); Fuel Cells and Hydrogen; Aeronautics; Embedded Computing Systems; and GMES (global monitoring for environment and security).

The Innovative Medicines Initiative (IMI)[76] is one such JTI, a joint undertaking between the European Union and EFPIA (the European Federation of Pharmaceutical Industries and Associations). IMI is Europe's largest public-private initiative and aims to speed up the development of better and safer medicines for patients, including medicines to combat and treat cardiovascular disease. It supports collaborative research projects and builds networks of industrial and academic experts with the goal of increasing pharmaceutical innovation in Europe. While more general in nature than the specific nano-based activities in the NMP above, there are still be a number of possibilities to use nanotechnology in the research and development work of Initiative. Projects relevant to work on health and nanotechnology include:

- Chem21: Chemical manufacturing methods for the 21st century pharmaceutical industries;
- MARCAR: Biomarkers and molecular tumour classification for non-genotoxic carcinogenesis;
- Onco Track: Methods for systematic next generation oncology biomarker development;
- SAFE-T: for safer and faster evidence-based translation of research; and
- WEB-RADR: to help in recognising adverse drug reactions.

ENIAC[77], the JTI in the area of nano-electronics also covers health applications. The ENIAC Joint Undertaking was established in February 2008 to co-ordinate European nano-electronics research activities through competitive calls for proposals. It describes itself as a public-private partnership in nano-electronics strengthening European competitiveness and sustainability, bringing together the ENIAC member states, the European Commission and AENEAS, the association of R&D actors in the field. Partners in ENIAC are working on projects under the Sub-Programme for Nano-electronics for Health and Wellness in areas including:

- DeNeCor, a consortium of 22 companies and research organisations across seven Member States, co-ordinated by Philips Medical Systems in the Netherlands and working on devices for neuro-control and neuro-rehabilitation relevant to neurodegenerative diseases, with a budget of EUR 19.9 million in 2013-2016;
- CAJAL4EU: a consortium of 29 organisations across eight Member States, co-ordinated by NXP Semiconductors and working on miniaturised biosensor technology platforms enabling diagnostic test manufacturers to build multi-parameter in-vitro test applications rapidly in a robust, user-friendly and cost-effective way, with a budget of EUR 22.6 million in 2010-2013; and
- CSI: a consortium of 15 organisations across four Member States, co-ordinated by STMicroelectronics and working to develop a low-cost medical-imaging platform for scanning the central nervous system, to be used in hospitals or in the patient's home, to improve the efficiency of diagnosis and therapy, with a budget of EUR 14.64 million in 2010-2013.

[75] http://era.gv.at/directory/142
[76] http://www.imi.europa.eu/
[77] http://www.eniac.eu/web/index.php

Working in related areas and using nano-electronics for health and other applications was the ARTEMIS JTI[78] that merged into another JTI, ECSEL, in 2014. The ARTEMIS[79] Industry Association has remained, representing actors in embedded and cyber-physical systems within Europe. The association represents industry and the public sector (large companies, SMEs, universities and research institutes) in the ECSEL JU.

The Joint Technology Initiative for Electronic Components and Systems for European Leadership (ECSEL)[80] is a public-private partnership organisation in electronic components and systems. Its consortia are collaborating on projects to develop smart systems, systems and components for smart energy, smart cities, smart governance and smart living, including health.

4.3.2 EU policies and programmes: Health

Within the EU, policies related to nanotechnology are generally divided into policies for research (R&D) and policies for the safety of the worker and the citizen. Thus, nanotechnology research and development falls largely into the domain of those responsible for research policy (and, to some extent, industry policy) and nano-safety with those responsible for environmental protection.

In addition to the Framework Programmes, health research was supported in 2008-2013 through the Second Programme of Community Action in the Field of Health. It has a budget of EUR 321.5 million and aimed to improve citizens' health security in its response to disease and health threats; improve patient safety; promote health and reduce health inequality; and generate and disseminate health information, knowledge and best practice. It is in the last of these that the connection to scientific research is most clearly seen.

To assist in delivering the EU Health Strategy to 2020 *Together for Health*[81], health research in 2014-2020 is being supported through the Third Health Programme[82]. The overall aims of the Programme are to:

- Promote health, prevent diseases and foster supportive environments for healthy lifestyles taking into account the 'health in all policies' principle;
- Protect Union citizens from serious cross-border health threats;
- Contribute to innovative, efficient and sustainable health systems; and
- Facilitate access to better and safer healthcare for Union citizens

In 2014-2020, the Programme has a budget of EUR 449.4 million.

In all its priority areas, the Programme highlights the need for a health information and knowledge system to contribute to evidence-based decision-making. Research and innovation activities would support that, not least the research from the Framework Programmes. Some of that research would relate to nanotechnology but it is difficult to identify support for nanotechnology-related research in health policy. Rather the policies are focused on health, no matter which technology may offer useful results.

In addition to research in bringing results to the patient, research is also important in providing the evidence base to ensure the protection of the citizen and in preventing nano-related health issues. The topic of environmental health and safety is covered in more detail in the later section on "The wider environment: regulation, environmental health and safety".

4.3.3 EU policies and programmes: Structural and Investment Funds

Four (out of five) European Structural and Investment Funds (ESI Funds) provide support to research and innovation activities:

- The European Regional Development Fund (ERDF), for economic regeneration and safeguarding employment. Its main priorities are the support of small to medium-sized enterprises; the

[78] http://www.artemis-ju.eu/home_page
[79] https://artemis-ia.eu/about_artemis.html
[80] http://www.ecsel-ju.eu/web/index.php
[81] http://ec.europa.eu/health/strategy/policy/index_en.htm
[82] http://ec.europa.eu/health/programme/policy/index_en.htm

creation of a low carbon economy; research and innovation; information and communications technology; environmental protection, climate change adaptation, risk prevention and management, transport and social inclusion.
- The European Social Fund (ESF), for the enhancement of employment opportunities, social inclusion and skills. It supports skills and training; access to employment for all including women and migrants; improvement of public services; innovation in SMEs and access to start-up capital.

The ERDF and ESF together have a budget of about EUR 280 billion over 2014-2020.

- The European Agricultural Fund for Rural Development (EAFRD), which aims to strengthen the links between agriculture, food production and forestry and those performing research and innovation activities. Groups of collaborators are funded under the European Innovation Partnership on Agricultural Productivity and Sustainability. The Fund has a budget of EUR 95.6 billion over 2014-2020.
- The European Maritime and Fisheries Fund (EMFF) with a budget of EUR 6.4 billion over 2014-2020 for the development of businesses through research and innovation. It can also fund research studies for the development of policies for the management of fisheries.

The first two ESI Funds above are the ones most relevant to health and nanotechnology, albeit that the topic is likely to capture only a small part of their budget, particularly in comparison with the funding under the Framework Programmes and the NMP theme in particular.

4.3.4 EU policies and programmes: Cohesion funds

SMART SPECIALISATION AND REGIONAL RDI POLICY

The European Union's Cohesion Policy aims to reduce differences between regions in Europe and to ensure growth across the continent. Structural Funds are among the main tools to implement the policy, and it is within this framework that smart specialisation was introduced. The Smart Specialisation Strategies (RIS3) [83] are agendas for transformation by focusing regional innovation policies on regional priorities based on existing areas of strength, competitive advantage, and potential for excellence in each region.

Smart Specialisation is about identifying the unique characteristics and assets of each country and region, highlighting each region's competitive advantages, and aligning the regional stakeholders and resources around an excellence-driven vision of their future. It aims to:

- Focus policy support and investments on key national/regional priorities and challenges;
- Build on each country/region's strengths, competitive advantages and potential for innovation excellence;
- Exploits potential synergies with other countries and regions;
- Support all forms of innovation, encourage innovation and experimentation; and
- Stimulate private sector investment.

The next section considers Member State supports for health research and innovation through nanotechnology.

[83] http://s3platform.jrc.ec.europa.eu/eye-ris3. As of December 2015, 260 regions and countries that prioritise KETs; out of these there are seven regions that have set a priority in nanotechnology.

5 POLICIES AND PROGRAMMES IN MEMBER STATES FOR NANOTECHNOLOGY AND HEALTH

While European funding is important for many researchers, it makes up only about 8% of total public funding for R&D in the European Union. Member States channel the remaining 92% into national research and development, mostly retaining it within their own borders. However, much of that funding is employed in projects the results of which feed into European networks and collaborations. As Member States chose to prioritise nanosciences and nanotechnologies for funding at European level, it is hardly surprising that they largely have the same view at national level. While some countries fund nanotechnology R&D as a designated priority area others choose to integrate it into broader programmes.

For health, specific initiatives at Member State level, past[84] or present, include:

Austria: The Austrian NanoInitiative[85] (2004-2011, total funding EUR 70 million, administered by the Austrian Research Promotion Agency (FFG)), nanomedicine being one of nine priority areas. The initiative works on a collaborative basis across Austria and transnationally with consortia of research institutes, universities and firms working on problem-driven basic research questions with a medium-term perspective (5-7 years). The focus of the programme, matching the remit of its funding agency FFG, has been to invest in projects with considerable market potential, relevant to Austrian companies. The type of activities begun under the programme are now continuing under the thematic areas FFG's research funding programmes.

The Czech Republic: Healthy and Quality Life is one programme within the National Research Programme II (NRP II) adopted by the Czech Government on 9 March 2005. NRP II supported research projects in the period 2006-2011 with a budget of EUR 99.5 Million. It was a problem-oriented, applied research programme co-financed by industry. One of the programme areas was 'Nanomaterials in biology and medicine'. Under the areas of 'Genomics and proteomics of cell differentiation in oncological diseases' and 'Development of new diagnostic tools based on molecular-biological methods', funding was given to cancer research. A further thematic area of relevance was 'Genomics, proteomics and pathophysiology of cardiovascular diseases'.

Denmark: Under the Danish Council for Strategic Research, the Programme Commission on Strategic Growth Technologies[86] has had annual calls of total annual value approximately EUR 10 million for research projects on nanotechnology, biotechnology and information- and communication technology. The programme is now managed by the Innovation Fund Denmark. Between 2005 and 2010, EUR 116 million has been allocated to strategic research centres, research alliances and research projects, EUR 62 million being for nanotechnology, biotechnology and ICT. Among the strategic research centres funded under the programme is a Centre for Nano-vaccines[87]. The centre was established by the Statens Serum Institut in cooperation with the University of Copenhagen, Forschungs-Zentrum Borstel, Germany and Lund University in Sweden with the aim of developing vaccines for diseases including influenza and tuberculosis.

France: The French Agence National de la Recherche (ANR) channels public funding into priority areas including Nanotechnologies & Nanosystems for Health. The EUR 35 billion economic stimulus package Investissements d'Avenir (Investments for the Future) was launched at the end of 2009 and, since 2011, one priority for funding administered by the ANR has been nano-biotechnologies, especially in health and environmental research. In aiming to support scientific research, accelerate the transfer of research to clinical trials and to patients and to consolidate knowledge about toxicology and nanomaterials, the programme is funding therapies, imaging, diagnostics and medical devices base on nanotechnology and biotechnology.

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[84] FinNano, the Finnish nanoscience and nanotechnology programme, was established in 2005 and is coordinated jointly by Tekes and the Academy of Finland. Over EUR 120 million were invested by the programme between 2005 and 2010, with the aim of providing support across the whole innovation chain from basic research to commercial products. One priority area of the programme was the application of nanotechnology for Health and Well-being. More recently, Finland has moved away from specific funding of nanotechnology activity.

[85] https://www.ffg.at/nano-das-programm

[86] http://en.innovationsfonden.dk/strategic-research/

[87] http://www.nano-vaccine.org/

Germany: Germany was the first country in Europe to recognise a need for specific funding measure for nanomedicine, introducing the lead innovation programme "NanoforLife" as early as 2005. In 2011, the German Ministry for Education and Research (BMBF) published the Action Plan Nanotechnology 2015, outlining the strategy for responsible development, innovation and public dialogue for the period 2010-2015. The plan included proposals for developing nanotechnology in five main areas including health. In parallel, a new funding instrument was launched - Innovation Alliances - to provide funding for strategic co-operation between industry and public research in key technology areas that demand a large amount of resources and a long time horizon, but promise considerable innovation and economic impacts. Public funds and funding from the industry is combined in a typical proportion of 1:5 (public: private). One such health Innovation Alliance "Molecular Imaging for Medical Engineering" (nanotechnology) was formed by Bayer Schering Pharma AG, Boehringer Ingelheim Pharma GmbH & Co. KG, Carl Zeiss AG, Karl Storz & GmbH Co. KG and Siemens AG. They aim to create new diagnostic agents and imaging procedures for clinics and to develop pharmaceuticals.

Portugal: The International Iberian Nanotechnology Laboratory[88] was established as the result of a joint decision of the Governments of Portugal and Spain, in November, 2005. It is an international research organisation in the field of nanoscience and nanotechnology. Established as an Intergovernmental Organisation (IGRO), with a remit independent of national governments, the INL is developing itself into a state-of the art research environment (including nanofabrication facilities) for nano-biotechnology, nano-electronics, nanomedicine and materials science at nanoscale. In addition to being a facility for researchers in Portugal and Spain, it hosts those from non-EU countries such as Brazil. Amongst the key research activities at INL is nanomedicine and, in particular, the study, design and fabrication of nanoscale structures and devices for the diagnosis, treatment, and prevention of diseases and genetic disorders. Another key area is research in environment monitoring, security and food quality control which is being used to create better packaging and healthier foods.

The Netherlands: Innovation policy in the Netherlands is implemented through, *inter alia*, the Top Sectors policy[89] [90]. Businesses, researchers and government work closely together in Top consortiums for Knowledge and Innovation (TKIs). One of the nine top sectors is High Tech Systems and Materials with its roadmap on nanotechnology (implemented by TKI NanoNext) as an enabling and cross-cutting technology. The aim of the roadmap is to enable research that will lead to new applications to address the challenges that society currently faces. The technologies (for example, relating to materials, electronics/optics and sensors) can be deployed in multiple application areas (such as lighting, energy, health, water). The nanotechnology roadmap is also relevant to other top sectors, including Life Sciences and Health.

The United Kingdom (UK): The main player in UK policy measures related to nanotechnology as a key enabling technology (KET) is the Department for Business, Innovation and Skills (BIS) and its agency, the Technology Strategy Board, now called Innovate UK[91]. It supports SMEs with high growth potential, manages the Small Business Research Initiative[92] and identified future potential growth sectors and commercialisation opportunities. Under this industry-focused policy, Innovate UK has co-funded industry research and development on projects on nanotechnology and on health, and specifically one on Magnetic Nanotechnology for Cancer Treatment.

The UK Enabling Technologies Strategy 2012-2015[93] also addressed four enabling technologies - advanced materials; biosciences; electronics, sensors and photonics; and information and communication technology (ICT) to support business in developing high-value products and services in areas such as energy, food, healthcare, transport and the built environment. Nanotechnology is identified as having a significant underpinning role across most of these technology areas, particularly in the healthcare and life sciences sectors.

[88] www.inl.int
[89] http://www.hollandhightech.nl/nationaal/innovatie/roadmaps/smart-industry
[90] http://www.hollandhightech.nl/nationaal/innovatie/roadmaps/nanotechnology
[91] https://www.gov.uk/government/organisations/innovate-uk
[92] https://www.gov.uk/government/collections/sbri-the-small-business-research-initiative
[93] https://www.gov.uk/government/publications/enabling-technologies-strategy-2012-to-2015

Many Member State nanotechnology policies and programmes are identified in the table at the end of this section. There is also additional information in the Annex: *Additional Information on Member State Policies and Programmes* (an Annex which is common to all the NanoData Landscape Compilation reports).

In addition to individual Member State initiatives, there are bilateral and multilateral collaborations between countries, agencies and research organisations. National websites also highlight the importance nanotechnology for and some countries actively promote themselves as leaders in nanotechnology and health:

- From the Netherlands, the web site of Holland Trade (http://www.hollandtrade.com/): "The development of high-tech systems and materials is a key industry in the Netherlands. Micro and nanotechnology are important sources of employment, focusing on technological advancement….. Some examples of relevant applications of nanotechnology are: *early tracing of viruses, checking and dosage in the delivery of medicines, development of intelligent surgical appliances,* development of ultra-thin coatings …".
- The Research in Germany web site (http://www.research-in-germany.de/): "Nanotechnologies are a horizontal sector with many possible applications in …. energy technology, environmental technology or information technology as well as *health*. They hold great technological and economic potential for Germany. Today, about 1000 companies work on the development, application and distribution of nanotechnology products…".

Some of the policies and programme for nanotechnology, and where appropriate nanotechnology and health, in countries outside of the EU are reported in the next section.

Table 5-1: Member State policies and programmes for nanotechnology

Country	Name of Initiative	Dates	Relevance	Description	Target Groups	Implementing Body	Budget (EUR millions)
AT	Austrian NANO Initiative[94] (NANO)	2004-2011	Directly Targeting NT	Multiannual, funding collaborative R&D, co-ordinating NANO-related policy measures at national and regional levels. Since 2012, NT is supported via FFG's thematic research funding e.g. Production of the Future	IND SME HEI PRO	FFG	70 over 8 years
AT	------	From 2012	Thematic, not NT specific	Since 2012, NT R&D is being supported via FFG's thematic research funding e.g. Production of the Future	All	FFG	450 for all disciplines (over the preceding 4 years when funding was managed by BMVIT)
CZ	National Research Programme II (NRP II) - Healthy and Quality Life	2006-2011		Healthy and Quality Life within NRPII, is a problem-oriented programme, more focused on applied research (co-financed industry).	IND SME HEI PRO		99.5 over 6 years
DK	Strategic research in growth technologies[95]	From 2005	Directly Targeting NT	Programme to strengthen research at the bio-nano-ICT interface for socio-economic benefit	IND SME HEI PRO	Innovation Fund Denmark	c. 10 per annum
FI	FinNano[96]	2005-2009	Directly Targeting NT	Multiannual funding for nano S&T to study, exploit and commercialise nano.	IND SME HEI PRO	Tekes	70 over 5 years
FR	PNANO P2N	2002-5 2006 - 13	Directly Targeting NT	R&D on • Nanotechnologies, Nano-devices, Micro-Nano-systems • Simulation and modelling of nano-systems • Nanotechnologies for biology, health and agro-food • Nanotechnologies for energy and	IND SME HEI PRO and individuals	ANR[97]	139.8 for P2N over 8 years

[94] https://www.ffg.at/nano-aktuell ; https://www.ffg.at/11-ausschreibung-produktion-der-zukunft
[95] http://innovationsfonden.dk/en/about-ifd
[96] www.tekes.fi
[97] http://www.agence-nationale-recherche.fr/

Country	Name of Initiative	Dates	Relevance	Description	Target Groups	Implementing Body	Budget (EUR millions)
				environment • Integrative research projects for nano-systems			
FR	Investissements d'avenir (nanobiotech)	From 2011	Directly Targeting NT	Within the overall programme, nanobio is targeted especially for health and environmental applications	IND SME PRO	ANR	12 per annum
DE	Nanotechnology Conquers Markets	2004-2006	Directly Targeting NT	Five leading-edge innovation programmes including NanoforLife – pharmaceuticals and medical	All	BMBF	24 over 3 years
DE	Nano Initiative – Action Plan	2006-2010	Directly Targeting NT	Cross-departmental initiative led by BMBF: to speed up the use of the results of nanotechnological research for innovations; introduce nanotechnology to more sectors and companies; eliminate obstacles to innovation by means of early consultation in all policy areas; and (4) enable an intensive dialogue with the public.	All	BMBF	640 over 5 years
DE	Innovation Alliances	2007-2012	Directly Targeting NT	For strategic long-term co-operation between multiple industry and public research partners. Funds R&D, other innovation-related activities. Public and private funds are combined in a 1:5 ratio.	All	BMBF	500 over 6 years
NL	NanoNed	2004-2011	Directly Targeting NT	NanoNed was organised into eleven independent flagships based on regional R&D strength and industrial relevance, including the programme for fluidics investigating into clinical diagnostics.	IND SME HEI PRO and individuals	Dutch Ministry for the Economy	235 over 8 years
NL	NanoNextNL	2011-2015	Directly Targeting NT	Consortium-based system (over one hundred companies, nine knowledge intensive institutes, six academic medical centres and thirteen universities). Stakeholders collaborate on fundamental and applied research projects.	IND SME HEI PRO and individuals	Dutch Ministry for the Economy	125 over 5 years

Country	Name of Initiative	Dates	Relevance	Description	Target Groups	Implementing Body	Budget (EUR millions)
PT	International Iberian Nanotechnology Laboratory	2005 to date	Directly Targeting NT	International research organisation in the field of nanoscience and nanotechnology, the result of a joint decision of the Governments of Portugal and Spain. Becoming a state-of the art research environment (including nanofabrication facilities) for nano-biotechnology, nano-electronics, nanomedicine and materials science at nanoscale. INL hosts researchers from the EU and non-EU countries including Brazil.	IND SME HEI	Governments of Portugal and Spain	
ES	Strategic Action of Nano Science, Nano technologies, new materials and new industrial processes	2008-2011	Directly Targeting NT	To enhance the competitiveness of industry by generating new knowledge and applications based on the convergence of new technologies, where nanotechnology plays a central role.	IND SME HEI PRO	Ministry	33 over 4 years
UK	Micro and Nanotechnology Manufacturing Initiative[98]	2003-2007	Directly Targeting NT	Support for collaborative R&D and capital infrastructure, co-financed by industry	Industry	DTI	329 over 4 years, over 100 from public funds
UK	UK Nanotechnologies Strategy	2009-2012	Directly Targeting NT	Targets the ways by which nanotechnologies can address major challenges facing society such as environmental change, ageing and growing populations, and global means of communication and information sharing.	IND SME HEI PRO	TSB, EPSRC, BBSRC and MRC	
UK	Key Enabling Technologies Strategy	2012-2015	NT as Underpinning Technology	Addresses four enabling technologies - advanced materials; biosciences; electronics, sensors and photonics; and information and communication technology (ICT) to support business in	Business mainly	Innovate UK	GBP 20m a year in higher-risk, early-stage innovation across advanced

[98] http://www.innovateuk.org/

Country	Name of Initiative	Dates	Relevance	Description	Target Groups	Implementing Body	Budget (EUR millions)
				developing high-value products and services in areas such as energy, food, healthcare, transport and the built environment. Nanotechnology is identified as having a significant underpinning role across most of these technology areas, particularly in the healthcare and life sciences sectors.			materials; biosciences; electronics, sensors and photonics; and ICT

6 POLICIES AND PROGRAMMES IN OTHER COUNTRIES[99]

6.1 Europe

6.1.1 Non-EU Member States

6.1.1.1 Norway

From 2002 to 2011, Norway addressed nanotechnology for health through its Programme on Nanotechnology and New Materials (NANOMAT)[100]. In 2012, a follow-on programme to run until 2021 was initiated, the Nanotechnology and Advanced Materials Programme (NANO2021)[101]. Managed by the Research Council of Norway[102], this large-scale programme covers research on nanoscience, nanotechnology, micro-technology and advanced materials. The programme is designed to further raise the level internationally of the Norwegian knowledge base in nanotechnology and advanced materials. NANO2021 receives funding from the Ministry of Education and Research and the Ministry of Trade and Industry. The annual budget in the period 2013-2021 has been set at NOK 92.1 million (EUR 10 million[103])[104].

Within thematic priority area three of NANO2021, the programme addresses nanoscience, nanotechnology, micro-technology and advanced materials 'for improving health and new medical technology'.

6.1.1.2 Russia

The Russian Federation came comparatively late to nanotechnology as a topic for research, development and innovation policy. It was only in 2007 that a comprehensive government effort in the field began, with the launch in April of that year of a strategy for the development of the 'nano-industries'. The strategy was to be realised through a series of Federal Target Programmes, amongst which was one specifically dedicated to the development of nanotechnology and the creation of new government bodies for that purpose. The main focus of Russian nanotechnology efforts since that time has been on the development of a domestic infrastructure for nanotechnology research and development as well as for innovation, commercialisation and manufacturing of nano-products. This is expected to remain the major theme for the coming years.

State institutions have been the principal actors in the field of nanotechnology in Russia for the intervening period. The State corporation, RUSNANO, has had primary responsibility for the development of nanotechnology innovation and its commercialisation. RUSNANO was the outcome of a reorganisation in 2011 of the State "Russian Corporation of Nanotechnologies" that was established in 2007. It was set up as one of several state corporations intended to lead the economic modernisation that was proposed in the '*Concept for the Long-Term Socio-Economic Development of the Russian Federation'*.

RUSNANO now combines an open joint-stock company and a Fund for Infrastructure and Educational Programmes (FIEP). It had capital funding in 2008-2009 of over USD 4 billion (EUR 2.8 billion[105]) but this dropped to USD 2.6 billion (EUR 1.9 billion[106]) by the end of 2010, falling further thereafter. A gradual privatisation of RUSNANO began in 2011. The mission of RUSNANO is to grow the national nanotechnology industry through the commercialisation of nanotechnology and the co-ordination of nanotechnology-related innovation. It acts as a co-investor in nanotechnology projects having substantial economic or social potential.

RUSNANO has a very wide range of activities spanning from research to foresight to infrastructure, education, standards and certification. Its research projects fall under six clusters, one of which is medicine and biotechnology, a sector which took about 9% of its total funding between 2007 and

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[99] The UN method of classifying countries by macro geographical (continental) regions and geographical sub-regions was followed (http://unstats.un.org/unsd/methods/m49/m49regin.htm)

[100] http://www.forskningsradet.no/prognett-nano2021/Artikkel/About_the_programme/1253970633592?lang=en

[101] http://www.forskningsradet.no/servlet/Satellite?c=Page&pagename=nano2021%2FHovedsidemal&cid=1253969916237&langvariant=en

[102] http://www.forskningsradet.no

[103] At the exchange rate, October 2015

[104] Nanotechnology and Advanced Materials – NANO2021: Work Programme

[105] Average yearly conversion rate, 2008-2009 (*source*: www.wolframalpha.com)

[106] Average yearly conversion rate, 2010 (*source*: www.wolframalpha.com)

2011.

6.2 The Americas

6.2.1 North America

6.2.1.1 Canada

Nanotechnology is promoted in Canada mainly at the level of its Provinces, for example in Alberta and Quebec.

Alberta

The National Institute for Nanotechnology (NINT) is a research institution located in Edmonton on the main campus of the University of Alberta. Its primary purpose is nanotechnology research. The institute was established in 2001 as a partnership between the National Research Council of Canada (NRC), the University of Alberta and the Government of Alberta. As an institute of the NRC, its core funding comes from the Government of Canada and additional funding and research support from the university, the Government of Alberta and various federal and provincial funding agencies.

Following the announcement in 2007 of the Government of Alberta's Nanotechnology Strategy, nanoAlberta was created as an implementation organisation for that Strategy. NanoAlberta provides leadership to and co-ordination of the Province's wide range of capabilities, organisations and individuals with the aim of gaining a return of CND 20 billion (EUR 13.4 billion[107]) in market share for nano-enabled commerce by 2020.

Quebec

NanoQuébec is a not-for-profit organisation funded by the MEIE (Ministère de l'Économie, de l'Innovation et des Exportations du Québec). Its mission is to strengthen nanotechnology innovation, increase its diffusion and raise both capabilities and capacities in the Province in order that Quebec becomes a centre of excellence for nanotechnology. The overarching and long-term aim is that of maximising economic impacts from nanotechnology in Quebec. Since December 2014, following a merger with the Consortium Innovation Polymères, NanoQuébec has formed part of Prima Québec, Quebec's advanced materials research and innovation hub.

Quebec's Nano Action Plan 2013-2018[108] specifically targets four priority sectors: microsystems, health, industrial materials and forestry. It covers infrastructure, financing of innovation, knowledge transfer and technology transfer, and national and international outreach horizontally across the four priority areas.

Via a central point, QNI or Quebec Nanotechnology Infrastructure, it co-ordinates and provides infrastructure for 300 experts using a fund of CND 300 million (EUR 200 million[109]). QNI has particular strengths in micro-nanofabrication, characterisation, synthesis and modelling. Other infrastructure can be accessed but is not funded via QNI.

The Action Plan has also led to the financing of technological feasibility projects (maximum 6 months); collaborative industry/university research projects (1 to 2 years); and international research projects with strategic NanoQuébec partners. Knowledge and technology transfer are supported through training, industry internships, and dissemination and awareness activities; by establishing networks and by organising interactive visits by experts. Outreach actions aim to attract new projects and finance to Quebec and to increase the engagement in international projects by people from Quebec.

6.2.1.2 The United States of America (US)

The National Nanotechnology Initiative[110] was launched in 2000 across a group of eight Federal agencies with some responsibility for nanotechnology research, application and/or regulatory activity, and has grown to include 25 Federal agencies. It aims to create collaborations and bring together expertise to work on shared goals, priorities, and strategies thereby leveraging the resources of the participating agencies. The goals of the NNI Goals are to advance world-class

[107] Current conversion rates, October 2015
[108] http://www.nanoquebec.ca/media/plan-action_en1.pdf
[109] Current conversion rates, October 2015.
[110] http://www.nano.gov/

nanotechnology research and development; foster the transfer of new technologies into products for commercial and public benefit; develop and sustain educational resources, a skilled workforce, and the supporting infrastructure and tools to advance nanotechnology; and support the responsible development of nanotechnology.

The NNI is managed within the framework of the National Science and Technology Council (NSTC), a cabinet-level council under the Office of Science and Technology Policy at the White House. The Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the NSTC facilitates planning, budgeting, programme implementation, and review across the NNI agencies. The National Nanotechnology Coordination Office (NNCO) was established in 2001 to provide technical and administrative support to the NSET Subcommittee, serve as a central point of contact for Federal nanotechnology R&D activities, and perform public outreach on behalf of the National Nanotechnology Initiative.

The NSET Subcommittee is composed of representatives from agencies participating in the NNI and NSET has Working Groups on Global Issues in Nanotechnology; Nanotechnology Environmental & Health Implications; Nano-manufacturing, Industry Liaison, & Innovation; and Nanotechnology Public Engagement & Communications. Health topics are considered, for example, under global issues, environmental health and safety, manufacturing and public engagement.

In February 2014, the National Nanotechnology Initiative released a Strategic Plan[111] outlining updated goals and "programme component areas" (PCAs). The goals focus on extending the boundaries of research; fostering the transfer of technology into products; developing and sustaining skilled people (with the right infrastructure and toolset) for nanotechnology; and supporting responsible development of nanotechnology. The PCAs include four Nanotechnology Signature Initiatives (NSIs): (i) nanotechnology for solar energy collection and conversion; (ii) sustainable nano-manufacturing nano-electronics for 2020 and beyond; (iii) nanotechnology knowledge infrastructure (NKI); and nanotechnology for sensors and sensors for nanotechnology, the PCAs for sensors and electronics being the most relevant to health nanotechnology. The other four PCAs are (i) foundational research; (ii) nanotechnology-enabled applications, devices, and systems; (iii) research infrastructure and instrumentation; and (iv) environment, health, and safety (EHS).

The NNI's budget supplement proposed by the Obama administration for Fiscal Year 2015 provided for USD 1.5 billion (EUR 1.2 billion[112]) of funding. Cumulative NNI investment since fiscal year 2001, including the 2015 request, totals almost USD 21 billion (EUR 17 billion[113]). Cumulative investments in nanotechnology-related environmental, health, and safety research since 2005 is nearly USD 900 million (EUR 680 million[114]). The Federal agencies with the largest investments are the National Institutes of Health (NIH), the National Science Foundation (NSF), the Department of Energy, the Department of Defence, and the National Institute of Standards and Technology (NIST).

Some of the above-mentioned institutions, like NSF and NIST, have areas dedicated to nanoscience and nanotechnology, but they do not have a specific health-sector focus. For instance, a fundamental part of NIST's mission is related to measurement sciences and standards development. However, NIST has subject areas that are linked to the health sector, such as nano-biotechnology, nanotechnology/environment, health & safety and nano-electronics and nanoscale electronics. NIST provides facilities to support production, through the Centre for Nanoscale Science and Technology (CNST)[115], established in 2007. The CNST facilitates the access to commercial state-of-the-art nanoscale measurement and fabrication tools through its NanoFab.

Another important actor active in nanotechnology is the NSF. This federal agency, with an annual budget of USD 7.3 billion (EUR 6.8 billion[116]) (FY 2015), funds approximately 24% of all federally supported basic research (except for medical sciences) conducted by America's colleges and universities[117]. As for NIST, NSF does not have a specific focus on health but advancing in the national health, prosperity, and welfare is one of its goals.

With particular reference to the health sector, NSF collaborates with the National Institutes of Health

[111] http://www.nano.gov/sites/default/files/pub_resource/2014_nni_strategic_plan.pdf
[112] Average yearly conversion rate, 2015 (*source*: www.wolframalpha.com)
[113] Average yearly conversion rate, 2001-2015 (*source*: www.wolframalpha.com)
[114] Average yearly conversion rate, 2005-2015 (*source*: www.wolframalpha.com)
[115] http://www.nist.gov/cnst/index.cfm
[116] Conversion rate, November 2015 (*source*: www.wolframalpha.com)
[117] http://www.nsf.gov/about/

(NIH)[118], whose primary focus is health instead[119]. Among the institutes, one particularly active in the field of nanotechnology is the National Institute of Biomedical Imaging and Bioengineering (NIBIB). Worth mentioning is the Intramural Research Programme that aims "to advance knowledge in imaging and bioengineering research using a combination of basic, translational, and clinical science and to develop training programmes in related fields."[120]

Another health-sector specific organisation, more explicitly active in nanotechnology is the National Cancer Institute (NCI) and its Alliance for Nanotechnology in Cancer. In its first five years, the Alliance has addressed the topic of nanotechnologies for the diagnosis, treatment and prevention of cancer. As a result, the Alliance was allocated another 5-years of financial cover "to generate new preventative, diagnostic and therapeutic approaches to cancer in areas where improvements cannot be realised using existing technologies"[121]. The next five years of the programme aim to: "rapidly advance new nanotechnology discoveries and speed their transformation into cancer-relevant applications in clinical practice; aid nanoparticle characterisation and standardisation of characterisation methods to enable technology transfer from university laboratories to companies that bring these technologies to patients; develop the next-generation of cancer researchers in the area of nanotechnology"[122]. Among the Alliance Programmes are the Centres of Cancer Nanotechnology Excellence, the Cancer Nanotechnology Platform Partnerships, and the Cancer Nanotechnology Training Centres.

Some of the above-mentioned institutions, such as the NCI and NIST, by collaborating with the US Food and Drug Administration (FDA), also created the Nanotechnology Characterisation Laboratory (NCL) to perform preclinical efficacy and toxicity testing of nanoparticles. The NCL facilitates "regulatory review of nanotechnologies for cancer therapies and diagnostics" [123]. It provides essential infrastructures and "characterisation services to nanomaterial providers and accelerates the transition of basic nanoscale particles and devices into clinical applications" [124]. The NCL inspired also an important joint initiative between the US and the EU. Indeed, on 1 July, the European Nano-Characterisation Laboratory (EU NCL), funded by H2020, was launched. The laboratory is a cooperative arrangement between Europe and the United States and the first European transnational infrastructure in nano-medicine. Its goal is twofold: sharing knowledge 1) between academia and industry should foster innovation and the competiveness of nano-medicine products[125] and 2) between the EU and the US should facilitate "the international harmonisation of analytical protocols and help standardise regulatory requirements for clinical evaluation and marketing of nano-medicine internationally" [126].

In additional to these Federal initiatives, there exist also several policy initiatives at State level[127]. Programmes for the promotion of nanotechnologies currently exist in 23 States. Notable examples are the Texas Emerging Technology Fund[128], the Oklahoma Nanotechnology Initiative[129], the Illinois Nanotechnology "Collaboratory"[130], and the Oregon Nanoscience and Microtechnologies Institute (ONAMI)[131]. The State-level organisations typically undertake some or all of the following activities: fostering collaboration on nanotechnology topics and challenges between researchers and research centres; higher education/industry joint projects; education and outreach; access to technology experts and infrastructure; early-stage funding and investment opportunities; technology transfer and commercialisation; and awareness raising in the community.

[118] https://obssr.od.nih.gov/scientific_areas/smartconnect_health.aspx
[119] https://www.nih.gov/about-nih/what-we-do/mission-goals
[120] http://www.nibib.nih.gov/Research/NIHNano
[121] http://nano.cancer.gov/
[122] http://nano.cancer.gov/
[123] http://ncl.cancer.gov/
[124] http://ncl.cancer.gov/
[125] https://ec.europa.eu/jrc/en/news/eu-ncl-launched
[126] https://ec.europa.eu/jrc/en/news/eu-ncl-launched
[127] http://www.nano.gov/initiatives/commercial/state-local
[128] http://gov.texas.gov/. As of October 2010, the Texas Emerging Technology Fund has given a total of UDS 173 million to 120 companies as well as UDS 161 million to educational institutions.
[129] http://www.oknano.com /
[130] http://nano.illinois.edu/collaboration/index.html
[131] http://onami.us/

6.2.2 South America

6.2.2.1 Argentina

A first initiative to foster nanotechnology in Argentina was established in 2003 when the national Science and Technology Secretariat started to organise research networks in the field. In 2004, the Secretariat, looked to address gaps in what was being done under the National Agency for Scientific and Technological Promotion (ANPCYT, Agencia Nacional de Promoción Científica y Tecnológica[132]), as a result of which four nanoscience and nanotechnology networks were approved in 2005, bringing together around 250 scientists. In the same year, the Argentinian-Brazilian Nanoscience and Nanotechnology Centre (CABN, Centro Argentino-Brasileno de Nanociencia y Nanotecnología) was created as a binational co-ordination body integrating research groups, networks of nanoscience and nanotechnology, and companies in Argentina and Brazil, in order to support scientific and technological research in the area and to improve the human and scientific resources of both countries.

The Argentinian Foundation for Nanotechnology (FAN)[133] was initiated also in 2005 by the Economy and Production Ministry, with the aim of stimulating training and developing technical infrastructure to promote advances in nanotechnology and the adoption of nanotechnology by industry. It also aimed to encourage the participation of researchers, institutions and companies from Argentina in international networks.

While previous national programmes had differentiated between funding for the public sector on the one hand (essentially the research networks) and the private sector on the other (projects of the FAN), the nano sectorial funds (FS-NANO) launched in 2010 provided funding to projects dedicated to basic and applied science via public-private partnerships.

In 2011, the Ministry of Science, Technology and Productive Innovation issues published the Argentina Innovadora 2020 (Innovative Argentina Plan 2020): National Plan of Science, Technology and Innovation. The plan is focused on three general-purpose technologies (nanotechnology, biotechnology and information and communication technology (ICT)) addressing, amongst other priorities, bio-nanomaterials for health.

6.2.2.2 Brazil

Systematic policy support for nanotechnology started in 2001, when the Brazilian Ministry of Science and Technology (MCT) through the Brazilian National Research Funding Agency (Conselho Nacional de Desenvolvimento Científico e Tecnológico or "CNPq") earmarked BRL 3 million (USD 1 million) (EUR 1.12 million[134]) over four years to form Co-operative Networks of Basic and Applied Research on Nanosciences and Nanotechnologies. Four national research networks were established - nanostructured materials; nano-biotechnology; molecular nanotechnologies and interfaces; and nano-devices, semiconductors and nanostructured materials. In late 2004, a network on Nanotechnology, Society and Environment was created independent of the formal funding mechanisms.

Since 1999, Brazil's national plan has comprised an annual budget and a four-year strategic plan (the Plano Plurianual or PPA). In 2003, the Ministry created a special division for the general co-ordination of nanotechnology policies and programmes whose work resulted in a proposal for specific nanotechnology-related funding. That proposal was taken up in the PPA in 2004-2007 which provided for BRL 78 million (c. USD 28 million) (EUR 22 million[135]) over 4 years for the Programme for the Development of Nanoscience and Nanotechnology. The aim of the programme was "to develop new products and processes in nanotechnology with a view to increasing the competitiveness of Brazilian industry" which it implemented by supporting networks, research laboratories and projects.

A review of the funding in the light of the 2004 Industrial, Technological and Foreign Trade Policy, the government reconsidered the original budget and increased Federal investment for 2005 and 2006 from the original USD 19 million (EUR 15 million[136]) for those two years to c. USD 30 million (EUR 24 million[137]). Ten new research networks - including health-relevant networks for nano-biotechnology, nano-biomagnetism, coatings, and microscopy – were set up to continue previous

[132] http://www.agencia.mincyt.gob.ar/frontend/agencia/fondo/agencia
[133] http://www.fan.org.ar/en/
[134] Average yearly conversion rate, 2001(*source*: www.wolframalpha.com)
[135] Average yearly conversion rate, 2004-2007 (*source*: www.wolframalpha.com)
[136] Average yearly conversion rate, 2005-2006 (*source*: www.wolframalpha.com)
[137] Average yearly conversion rate, 2005-2006 (*source*: www.wolframalpha.com)

research activities but linking more closely to broader industry, technology, and trade policies. Industrial policy helped to reinforce the strategic status attributed at national level to nanotechnology and its role in enhancing Brazil's competitiveness. Of particular important in the programmes were the development of qualified human resources, the modernisation of infrastructure and the promotion of university-industry co-operation.

In 2012, the Brazilian Ministry for Science, Technology and Innovation (MCTI) launched the SisNANO[138] initiative, enabling scientists throughout Brazil to conduct experiments at 26 "open" laboratories offering the very best equipment for research in nanotechnology. University students and staff can use the facilities free of charge – provided they submit a good research proposal – while scientists working in industry are able to access specialist equipment and expertise at highly subsidised rates. A platform for nano-biotechnology projects for Brazil's public health system (the Unified Health System (SUS)) is also worth mentioning. This platform, called NANOSUS, aims to develop, validate and prototype nano-biotechnological processes and products for the public health system.

In 2013, MCTI launched the Brazilian Nanotechnology Initiative (IBN) with funding estimated to be BRL 440 million (EUR 148 million[139]) for the 2013-2014 period. The implementation of IBN was an effort to further strengthen nanotechnology in Brazil by strengthening academic and industry linkages thereby to promote the scientific and technological development of the nanotechnology sector.

6.3 Asia

6.3.1 Eastern Asia

6.3.1.1 China

The transition of China from a centrally-planned to a more market-oriented economy, begun in the 1980s, has also led to greater decentralisation of the science and technology (S&T) system. Central government is increasingly co-ordinating S&T, rather than managing research and development (R&D) with research institutions taking on a greater role in policy, setting their own research agendas in the context of the National Five-year Plans.

The National High Technology Research and Development Programme (the 863[140] programme announced in 1986) focuses on key high technology fields of relevance to China's national development, supporting research and development, strengthening technological expertise and laying the foundations for the development and growth of high technology industries. Its goals are 'promoting the development of key novel materials and advanced manufacturing technologies for raising industry competitiveness' including nanomaterials. The programme is supervised by the National Steering Group of S&T and Education, and is managed by the Ministry of Science and Technology.

The 863 Programme is implemented through successive Five-Year Plans. In addition to nanotechnology research funding, the Tenth Five-Year Plan (2001-2005) targeted commercialisation and development of nanotechnology. The Government disaggregated nanotechnology development between short-term projects (development of nanomaterials), medium-term projects (development of bio-nanotechnology and nano medical technology), and long-term projects (development of nano electronics and nano-chips). The Eleventh Five-Year Plan (2007-2012) thereafter emphasised innovative technologies, including biological and aerospace industries, the development of new materials for information technology, and commercialising of the technology for 90-nanometer and smaller integrated circuits.

The 1997 "National Plan on Key Basic Research and Development" together with the "National Programme on Key Basic Research Project (973 Programme)" sought to strengthen basic research in line with national strategic targets[141]. The 973 Programme complements the 863 programme, funding basic research on nanomaterials and nanostructures (i.e. carbon nanotubes). The National Steering Committee for Nanoscience and Nanotechnology (NSCNN) was established in 2000 to coordinate and streamline all national research activities including overseeing the 863 and 973

[138] Sistema Nacional de Laboratórios em Nanotecnologias ftp://ftp.mct.gov.br/Biblioteca/39717-SisNANO.pdf
[139] Average yearly conversion rate, 2013-2014 (*source*: www.wolframalpha.com)
[140] The programme is named for its date, the 86 for 1986 and the 3 for the third month, hence 86/3 or 863. Likewise for the 973 programme launched in 1997.
[141] http://www.chinaembassy.bg/eng/dtxw/t202503.htm

programmes. The NSCNN consists of the Ministry of Science and Technology (MOST), the Chinese Academy of Sciences (CAS), the National Natural Science Foundation (NSFC), the National Development and Reform Commission (NDRC), the Ministry of Education (MOE) and the Chinese Academy of Engineering (CAE).

The Medium-and Long-term National Plan for Science and Technology Development 2006-2020 (MLP) aims to achieve the promotion of S&T development in selected key fields and to enhance innovation capacity. The MLP calls for more than 2.5% of GDP to be invested in R&D; for S&T to contribute at least 60% to economic growth; for dependence on foreign technologies to decrease to under 30%; and for China to rank in the top five in the world for patents and citations in international publications.

Nanotechnology is given priority status under the MLP, being seen as one of the Chinese 'megaprojects' in science. Specifically, R&D should be undertaken on nano drug carriers, nanomaterials and devices, design and manufacturing technology, nano-scale complementary metal-oxide semiconductor (CMOS) devices, energy conversion and environmental purification materials, and information storage materials. As the MLP is implemented in the context of the Five-Year Plan for S&T Development (2011-2015), it is relevant that it also emphasises key technologies for strategic and emerging industries (including nanotechnology with ICT, photonics, manufacturing and agriculture), and seeks to address not only energy and environmental needs but also those of the ageing population (pharmaceuticals, medical equipment) and thereby health nanotechnology.

In addition, China is promoting itself in nanotechnology. From http://www.china.org.cn/: "China is positioning itself to become a world leader in nanotechnology … Nanotechnology has many potential applications with significant economic consequences in industrial design, *medicine*, agriculture, energy, defence, food, etc. In medicine for example, these include nanoscale drug particles and delivery systems and nano-electronic biosensors…. Today, China leads the world in the number of nanotechnology patents".

6.3.1.2 Japan

Strategic prioritisation of nanotechnology started in Japan under the Second Science and Technology Basic Plan (STBP) 2001-2005. One of eight priority R&D topics of national important, nanotechnology and materials were identified alongside life sciences, ICT, energy, environmental sciences and manufacturing technology together with the cross-cutting areas of infrastructure and frontier research. Nanotechnology was seen as being relevant to a broad range of fields and it was expected to help Japan to maintain its technological edge. Total governmental funding of this field grew from JPY 85 billion (EUR 782 million)[142] in 2001 to JPY 97 billion (EUR 709 million[143]) in 2005.

In the subsequent STBP[144], which ran from 2006 to 2010, Japan established nanotechnology and materials as one of its four priority research fields, the others being life sciences; environmental sciences; and information and communications. Together with energy, environment, manufacturing and frontiers, these formed eight Promotion Areas. The total budget over the five years was JPY 250 trillion (EUR 200 billion[145]).

There were five sub-areas under nanotechnology and materials: nano-biotechnology and biomedical materials; materials; nano-electronics; fundamentals for nanotechnology and materials; and nanotechnology and materials science. Research in the nano-biotechnology and biomedical materials area included work on tissue engineering, nanomedicines, molecular imaging, next-generation drug delivery systems and bio-diagnostics for personalised medicine.

In 2010, a New Growth Strategy was introduced to combat the lengthy stagnation in the Japanese economy. The strategy sought to create jobs by tackling the issues faced by the economy and society. This took the form of a reorientation of priorities towards green innovation (reducing emissions and addressing climate issues), life innovation (healthy and long living, making Japan a health superpower), the Asian economy (issues of specific Asian concern including falling birth rates and

[142] Average yearly conversion rate, 2001 (*source:* www.europarl.europa.eu/RegData/etudes/note/join/2007/379231/IPOL-TRAN_NT%282007%29379231_EN.pdf)
[143] Average yearly conversion rate, 2006-2010 (*source:* www.europarl.europa.eu/RegData/etudes/note/join/2007/379231/IPOL-TRAN_NT%282007%29379231_EN.pdf)
[144] https://www.jsps.go.jp/english/e-quart/17/jsps17.pdf
[145] Average yearly conversion rate, 2006-2010 (*source:* http://www.europarl.europa.eu/RegData/etudes/note/join/2007/379231/IPOL-TRAN_NT%282007%29379231_EN.pdf)

ageing societies) and tourism and the regions. Growth-related strategies for ('making Japan a superpower in') science, technology and ICT, for employment and human resources, and for the financial sector were also identified as essential in supporting growth. The strategy also addressed the issues arising from the earthquake, tsunami and nuclear crisis of 2011.

These same issues were incorporated in 2011 into the Fourth Science and Technology Basic Plan (2011-2015) with a budget of EUR 250 billion (JPY 25 trillion). As with the New Growth Strategy, and in contrast to the previous Basic Plan for Science and Technology, the Fourth Basic Plan shifted away from emphasising technologies towards "demand driven and solution-oriented topics" as well as to "problem solving and issue-driven policies" and the "deepening the relationship between society and science and technology." Two broad based areas are prioritised: Life Innovation and Green Innovation and an emphasis has been placed on technologies to reduce global warming, provision and storage of energy supply, renewable energies, and diffusion of such technologies. For health, innovative health care technologies, pharmaceuticals and devices are being promoted. As there is no specific emphasis on individual technologies, nanotechnology is incorporated across research and development without being specifically targeted.

In 2013, a new public-private partnership was launched to support the promotion and development of new health technologies. The Global Health Innovative Technology Fund was established by the Government of Japan, a consortium of Japanese industries, and the Bill and Melinda Gates Foundation to develop R&D partnerships and to fund R&D projects and partnerships.

6.3.1.3 Korea (South)

Long a topic of relevance in Korea, support for nanoscience and nanotechnology reached a new level in December 2000 with the announcement by the National Science and Technology Council (NSTC)[146] of the Korean National Nanotechnology Initiative (KNNI). Nanotechnology was also identified as one of six priority fields in the National Science and Technology Basic Plan (2002–2006). The NT Development Plan was approved by the NSTC on in July 2001 and the NT Development Promotion Act passed in November 2002 by the National Assembly. The initiative is now in its 3rd phase (2011-2020), with focus on 'clean nanotech'. Investment in phase 1 (2001-2005) was 105.2 billion Won (EUR 83 million[147]); phase 2, 277.2 billion Won (EUR 1,541.8 million[148]).

Under its KNNI, Korea has focused on establishing specific support mechanisms (programmes, systems and societies) and centres of excellence across the country. The launching of the National Programme for Tera-Level Nano-devices (2000) was followed by the founding of the Nanotechnology Industrialisation Support Centre (2001) and the Korean Advanced Nanofabrication Centre[149] (KANC) (2003). In more recent times, building on former centres, Korea established two NST centres at the Institute for Basic Science: the Centre for Nanoparticle Research and the Centre for Nanomaterials and Chemical Reactions (2012)[150]. In total, 24 nanotechnology-related centres now exist in Korea. The Korean Institute of Science and Technology (KIST)[151] has a Material and Life Science Division, covering nanotechnology, ICT and biotechnology.

Under the Nanotechnology Development Promotion Act 2002, Korea also established in 2004 the Korean Nano Technology Research Society (KoNTRS)[152] as a mechanism for co-operation between researchers working on nanotechnology throughout the country, to develop collaborative research programmes between institutions (public and private) and to support the government in establishing sound national NST policies.

Korea has since continued to invest in nanotechnology, with the review by NSTC in 2006 of the first five years of its NNI leading to support continuing for an additional ten years. In this third phase of the NT Development Plan (2011-2020), there is greater focus on clean nanotechnology and overall the policy has evolved, moving away from funding fundamental research towards more application-

[146] http://www.nstc.go.kr/eng/
[147] Average yearly conversion rate, 2001-2005 (*source*: www.ecb.europa.eu/stats/exchange/eurofxref/html/eurofxref-graph-krw.en.html)
[148] Average yearly conversion rate, 2006-2010 (*source*: www.ecb.europa.eu/stats/exchange/eurofxref/html/eurofxref-graph-krw.en.html)
[149] http://www.kanc.re.kr/kancEnglish/center/center_overview.jsp
[150] https://www.ibs.re.kr/eng/sub02_04_03.do
[151] KIST is a science and technology institute. It was the first S&T research institute founded in Korea following the joint statement by the Presidents of Korea and the US on the "Establishment of a Korean Industrial and Applied Science R&D Institute" (1966) http://eng.kist.re.kr/kist_eng/?sub_num=728
[152] http://kontrs.or.kr/english/index.asp

driven actions.[153]

Korea has also sought to develop its nanotechnology policy and policy system, with the production of the Korean Nanotechnology Roadmap in 2008 and the establishment of the National Nanotechnology Policy Centre (NNPC) in 2010. The NNPC announces on its web site[154] the national vision for Korea to be "the world's number one nanotechnology power" and the four goals:

- "To become a leading nation in nanotechnology with systematic nanotechnology R&D programmes;
- To create a new industry based on nanotechnology;
- To enhance social and moral responsibility in researching and developing nanotechnology; and
- To cultivate advanced nanotechnology experts and maximise the utilisation of nanotechnology infrastructure."

Mid-term and long-term strategies for nanotechnology in Korea which have been developed and implemented since about 2009 include:

- The Fundamental Nanotechnology Mid-term Strategy [NT 7-4-3 Initiative] through which the Ministry of Education, Science and Technology (MEST) supported 35 green nanotechnologies in seven areas as well as funding four infrastructure projects;
- The Nano Fusion Industry Development Strategy by MEST and the then Ministry of the Knowledge Economy (MKE) which sought to support nanotechnology all across the value chain, from the research laboratory to the marketplace;
- The National Nano Infrastructure Revitalisation Plan, also by MEST and MKE, to link nanotechnology infrastructures together thereby giving them new impetus; and
- The Nano Safety Management Master Plan 2012-2016 to define methods and processes for the identification and manage any safety risks that emerge with the development, commercialisation and manufacture of nanotechnology products.

2012 saw the creation of the Nano-Convergence Foundation (NCF)[155] whose remit is to increase the commercialisation of national NST research outcomes. It operates under the joint support of the Ministry of Science, ICT & Future Planning (MSIP) and the Ministry of Trade, Industry & Energy (MOTIE). Korea plans to invest 930 billion Korean Won (ca. USD 815 million, EUR 740 million[156]) by 2020 in the NST, with projects in the Nano Convergence 2020 programme each eligible to receive up to 2 billion Korean Won (EUR 1.5 million[157]).

6.3.1.4 Taiwan (Chinese Taipei)[158]

The National Nanoscience and Nanotechnology Programme[159] was approved for a period of six years by the National Science Council (NSC) in 2002. With a budget envelope of USD 700 million (EUR 740 million[160]) and actual expenditure estimated to be USD 625 million (EUR 486 million[161]) over 2003-2008, the aim of the programme was to foster nanotechnology research and development in research institutes, universities and private companies, achieving academic excellence and supporting commercialisation. The Academic Excellence part of the programme includes nano-biotechnology, as well as physical, chemical and biological properties of nanostructures, nanosensors (nanoprobes) and nanodevices. Industrial applications are the remit of the Industrial Technology Research Institute (ITRI). ITRI has 13 research laboratories and centres in areas including biomedicine, as well as chemistry, applied materials, electronics, optoelectronics, and mechanics.

The National Nanoscience and Nanotechnology Programme also co-ordinates the nanotechnology research efforts of government agencies mainly through the establishment of common core facilities and education programmes, by promoting technology transfer and commercialisation into industrial applications and establishing international competitive nanotechnology platforms. Among the thematic priorities of the programme overall have been the design and fabrication of interconnects, interfaces and system of functional nano-devices, the development of MEMS/NEMS technology, and

[153] http://www.nanotechmag.com/nanotechnology-in-south-korea/
[154] http://www.nnpc.re.kr/htmlpage/15/view
[155] http://www.nanotech2020.org/download/english_brochure.pdf
[156] Current exchange rate, November 2015 (*source*: www.wolframalpha.com)
[157] Current exchange rate (November 2015) (*source*: www.ecb.europa.eu/stats/exchange/eurofxref/html/eurofxref-graph-krw.en.html)
[158] http://www.twnpnt.org/
[159] http://www.twnpnt.org/english/g01_int.asp
[160] Average yearly conversion rate, 2002 (*source*: www.wolframalpha.com)
[161] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2768287/

nano-biotechnology.

Taiwan's Nanotechnology Community (NTC) was established in 2003 to identify commercial applications of nanotechnology and, in 2004, the Taiwan Nanotechnology Industrialisation Promotion Association (TANIPA) was set up by the Industrial Development Bureau at the Ministry of Economic Affairs (MOEA), with a strategic remit related to industrial applications of nanotechnology and to facilitate public-private co-operation.

Phase I of the National Nanoscience and Nanotechnology Programme was completed in 2008. Phase II was approved by the NSC in April 2008 to run for another six years (2009-2014) with the goal of strengthening and concentrating public resources on "Nanotechnology Industrialisation" i.e. the development of nanotechnology for domestic industry relevant to Taiwan and its growth into high-tech industry. Building on Phase I, Phase II has supported nano-biotechnology, nano-electrics, nano-optoelectronics, energy and environmental nanotechnology, nano-instrumentation, nano-materials, and applied nanotechnology in traditional industries.

6.3.2 Southern Asia

6.3.2.1 India[162]

The Nanomaterials Science and Technology Initiative (NSTI) was launched by the Ministry of Science and Technology's (MST) Department of Science and Technology (DST) in October 2001 to support priority areas of research in nanoscience and nanotechnology, strengthen national characterisation and infrastructural facilities, enhance nanotechnology education in order to generate trained manpower in the area, and create an applications-related interface between educational institutions and industry. The Indian government committed to investing USD 16 million (EUR 14 million[163]) in nanomaterials research and commercial development over the five-year duration of the initiative, 2002-2006. The funding was used for projects, centres of excellence, conferences and advanced courses (schools), and post-doctoral fellowships. Within its basic and application-oriented research programmes, it supported work on nanomaterials for pharmaceuticals and drug delivery, gene targeting and DNA chips.

A capacity-building programme for nanoscience and nanotechnology (called Nano Mission)[164] was announced in 2007. It was implemented by DST with a budget of EUR 155 million over 5 years. In that time, India raised its publication output in nano-science and –technology generating about 5000 research papers and about 900 PhDs directly from Nano Mission funding. Under the programme, scientists were given access global state-of-the-art facilities in countries including Japan and Germany. The programme is also seen as having resulted in products including nano hydrogel-based eye drops, pesticide removal technology for drinking water, water filters for arsenic and fluoride removal and nano silver based antimicrobial textile coatings. Finally, it facilitated discussions on standards for nanotechnology at national level.

The continuation of the Nano Mission was approved by the Government in February of 2014 and EUR 91 million (INR 650 crore) were sanctioned for the time period 2012 to 2017[165]. The programme will continue to support nanoscience and technology by promoting basic research, human resource development, research infrastructure development, international collaborations, national dialogues, and nano-applications and technology development. In the area of development of products and processes, the programme has focused, and will continue to focus, on areas of national relevance including sensor development, safe drinking water, materials development and drug delivery.

In addition to DST, several other agencies support nanotechnology research and development:

- The MST's Department of Biotechnology (DBT)[166] funds nano-biotechnology under its basic research programmes as well as having programmes on stem cell research and regenerative medicine, vaccines and diagnostics, and bioengineering that all involve nanotechnology directly or indirectly.

[162] http://www.oecd.org/science/nanosafety/37277620.pdf; http://nanomission.gov.in/; http://www.ris.org.in/images/RIS_images/pdf/DP%20193%20Amit%20Kumar.pdf, http://erawatch.jrc.ec.europa.eu/erawatch/opencms/information/country_pages/in/country?section=ResearchPolicy&subsection=ResPolFocus

[163] Average yearly conversion rate, 2002-2006 (*source*: www.wolframalpha.com)

[164] http://nanomission.gov.in/;

[165] http://timesofindia.indiatimes.com/home/science/Govt-approves-Rs-650-crore-for-Nano-mission/articleshow/30722422.cms

[166] http://www.dbtindia.nic.in/

- The Council of Scientific and Industrial Research (CSIR)[167] has a network of 38 laboratories and other partners involving about 4600 scientists in research and development across a wide range of disciplines including nanotechnology and for application areas including health, water, food and environment.
- In 2003, the CSIR launched the New Millennium Indian Technology Leadership Initiative (NMITLI) to foster public-private partnerships via grant-in-aid funding to public partners and soft loans to their industrial partners. The initiative specifically targeted nanosciences and nanotechnologies; biotechnology; energy and materials.[168]
- The CSIR's International Science and Technology Directorate (ISAD) facilitates nanotechnology workshops and projects in collaboration with partners from South Africa, France, South Korea, China and Japan[169].
- The MST's Science and Engineering Research Council (SERC)[170] supports frontier and interdisciplinary research. Support for nanotechnology projects has been provided through its R&D schemes for basic science and engineering science.

6.3.2.2 Iran[171]

The Islamic Republic of Iran ranked 23rd in the world in nanotechnology in 2007, second to Korea in citations in Asia[172], but, by 2012, it had moved to 10th place[173, 174]. In 2013, Iran ranked 20th in science production in the world (Thomson Reuters) and 18th in science production for medicine. According to the Ministry, its share of global science production rose from 1.39% in 2013 to 1.69% percent in 2014, as measured by indicators including the number of scientific papers, the quality and quantity of documents, patenting inventions, industrial plans, partnership with foreign universities, and the use of technology in domestic organisations.

There are nine scientific committees responsible for organising and coordinating science activities in Iran including committees for nanotechnology, biotechnology, aerospace, information technology, renewable energies and environment.

Iran began its nanotechnology activities with a Study Committee for Nanotechnology in 2001. Its work led to the development of the Iran Nanotechnology Initiative Council (INIC)[175], established in 2003 to develop policies to foster nanotechnology in Iran and monitors their implementation. The Council also funds researchers, having supported over 1400 researchers for nanotechnology activity between 2004 and 2010, at a cost of USD 12 million[176] (EUR 9 million[177]).

INIC has also funded the development of research and training facilities for nanotechnology research, such as the Institute for Nanoscience and Nanotechnology (INT) at the Sharif University of Technology. The INT, established in 2004, was the first institute to offer a PhD in nanotechnology in Iran[178]. INIC undertakes education and awareness-raising activities including a students' Nano Club, seminars, workshops, publications and a multi-lingual (Arabic, Persian, Russian and English) website[179].

Also in 2004, INIC was instrumental in establishing the Iran Nanotechnology Laboratory Network to optimise Iran's nanotechnology infrastructure. Forty-two laboratories across Iran operate under the network. The role of INIC includes evaluation and ranking of member laboratories and providing support for them in areas such as training workshops, lab equipment, and in gaining accreditation as testing and calibration labs.

INIC operates through working groups on areas including Human Resource Development; Technology Development and Production; and Education and Awareness. It also addresses standards and regulations through the Iran Nanotechnology Standardisation Committee (INSC)[180], a body

[167] www.csir.res.in/
[168] http://www.csir.res.in/external/heads/collaborations/NM.pdf
[169] http://www.teriin.org/div/ST_BriefingPap.pdf
[170] www.dst.gov.in/about_us/ar05-06/serc.htm
[171] See also http://www.sciencedev.net/Docs/Iran_Nano.pdf (2010)
[172] http://webarchive.nationalarchives.gov.uk/20090609003228/http://www.berr.gov.uk/files/file11959.pdf
[173] http://statnano.com/report/s29
[174] http://www.nanotech-now.com/news.cgi?story_id=45237
[175] http://nano.ir/index.php?lang=2
[176] http://www.nanotech-now.com/news.cgi?story_id=36557
[177] Average yearly conversion rate, 2004-2010 (*source*: www.wolframalpha.com)
[178] http://blogs.scientificamerican.com/guest-blog/science-and-sanctions-nanotechnology-in-iran/
[179] http://nano.ir/index.php?ctrl=static_page&lang=2&id=397&section_id=22
[180] http://nanostandard.ir/index.php?lang=2

established in 2006 as a collaboration between the INIC and the Institute of Standard and Industrial Research of Iran (ISIRI)[181].

Continuing to support nanotechnology and the work of INIC, a "Future Strategy" was adopted in 2005 by the Cabinet, a 10-year nanotechnology development (2005 - 2014). Its mission was to place Iran among the top fifteen advanced countries in nanotechnology in the world. The focus was placed on building and using infrastructure and human resources; improving communication and networking both within Iran and internationally; and generating economic added value from nanotechnology as a means of achieving economic development[182].

Internationally, in the context of the Economic Co-operation Organisation (ECO), Iran promoted the establishment in 2009 of an ECO Nanotechnology Network, both providing funding to establish the network and agreeing to co-ordinate it jointly with the ECO Secretariat. INIC is the Iranian representative on the network.

6.3.3 South-Eastern Asia

6.3.3.1 Malaysia

The Second National Science and Technology Policy (STP II), launched in 2003, identified nanotechnology as a priority emerging technology for Malaysia. Specific products and technologies specified included: photovoltaic (PV) solar cells, Li-ion batteries, plant vaccines, drug delivery systems, nano-biochips, and nano-biosensors.

The Malaysian National Nanotechnology Initiative (NNI) was established in 2006 to advance nanotechnology and related sciences by clustering local resources and knowledge of Malaysian researchers, industry and the government. The NNI paved way for the establishment in 2010 of the National Nanotechnology Directorate under the Ministry of Science, Technology and Innovation (MOSTI). The National Nanotechnology Directorate (NND)[183] facilitates nanotechnology development in Malaysia by acting as a central co-ordination agency.

To further support activity on these priority areas, the National Innovation Council of Malaysia in 2011 identified the need for a national organisation for nanotechnology commercialisation. NanoMalaysia[184] was created in 2011 as a company under the Ministry of Science, Technology and Innovation (MOSTI). It is responsible for commercialisation of nanotechnology research and development; industrialisation of nanotechnology; facilitation of investments in nanotechnology; and human capital development in nanotechnology.

In 2011, the Top down Nanotechnology Research Grant (NanoFund) was introduced and NanoMalaysia Centres of Excellence created. Among these are the Institute of Nano-electronics and Engineering (INEE)[185], UNIMAP[186] which focuses on Nano DNA Chips for medical diagnostics and the Institute of Micro Engineering and Nano-electronics (IMEN), UKM[187] which focuses on Nanoelectromechanical Systems (NEMS) and Lab on Chips for the biomedical industry.

6.3.3.2 The Philippines[188]

Nanotechnology was first identified as a priority area in the Philippines in 2009 when the Department of Science and Technology (DOST) formed a multidisciplinary group to create a roadmap for the development of nanotechnology in the country. The Nanotechnology Roadmap for the Philippines identified five key sectors for the application of nanotechnology that also coincided with the priority areas of DOST for R&D support. These areas were: health; environment; information and communications technology and semiconductors; food and agriculture; and energy.

6.3.3.3 Singapore

With the aim of transitioning to a knowledge-based economy, Singapore has relied since the early 1990s on its five-year basic plans for science and technology (S&T). Foresight and technology

[181] http://www.isiri.com/
[182] http://statnano.com/strategicplans/1
[183] http://www.mosti.gov.my/en/about-us/divisions-departments/national-nanotechnology-directorate-division-nnd/
[184] http://www.nanomalaysia.com.my/index.php?p=aboutus&c=whoweare
[185] http://inee.unimap.edu.my/
[186] www.unimap.edu.my/
[187] www.ukm.my/
[188] http://www.techmonitor.net/tm/images/d/d1/10jan_feb_sf3.pdf

scanning were key components of the process by which the 2010 plan[189] was developed. Thirteen technology scanning panels were established, one on 'Exploiting Nanotechnologies'. There were also panels on engineering science in medicine, materials and infrastructure, manufacturing, information storage, semiconductors, energy, environmental technologies, intelligent systems, broadband, the grid, information management, and frontiers in chemicals.

In the 2010 strategy document the connection is made between the S&T Plan and the Manufacturing 2018 Plan Intelligent National Plans of Singapore's Economic Development Board[190], and the Roadmap (ITR5) of the Infocomm Development Authority[191]. It links nanotechnology research and development to industrial development and supports collaboration between industry, research institutes and universities. The aim is for an enhancement of applied research in nanotechnology to enable industrial clusters including electronics, chemicals, food, precision machinery, transportation machinery, environmental engineering, and ICT. The Plan also indicates nanotechnology is fundamental and horizontal to these clusters.

Nanotechnology is one of six areas at the heart of clinical and translational research supported under the Biomedical Research Council, which is responsible for research related to the industrial sectors of pharmaceuticals, medical technology, biotechnology and healthcare services and delivery. Nanotechnology is also a key area for the Science and Engineering Research Council (SERC).

The principle funding agency for nanoscience and nanotechnology (NST) in Singapore is the Agency for Science, Technology & Research (A*STAR)[192]. A*STAR's Nanotechnology Initiative started in 2001 with the target of building on existing capabilities to develop specific areas of NST research always with applications and potential use by industry as a goal. A*STAR research institutes involved in NST include the Institute of Bioengineering and Nanotechnology (IBN)[193]; the Institute of Manufacturing Technology (SIMTech); the Institute of Materials Research and Engineering (IMRE)[194]; the Institute of Microelectronics (IME)[195]; and the Data Storage Institute (DSI)[196]. The research activities of IBN are focused in the areas of nanomedicine, synthetic bio-systems, bio-devices and diagnostics, and green chemistry and energy.[197]

In 2010, A*Star's SIMTech launched the Nanotechnology in Manufacturing Initiative (NiMI) to foster collaborative efforts between research and industry, developing industrial capability and enhancing competitiveness. The initial focus was on joining, forming and coating using nanotechnology, each of which can be applied in health nanotechnology. Other areas of application include automotive and electronics (e.g. manufacture of solders, carbon nanotubes, nanocomposites and their characterisation and application).

6.3.3.4 Thailand

Thailand has been active in nanotechnology since at least 2003 when it established NANOTEC[198] as the leading national agency for nanotechnology development. It operates under the jurisdiction of the National Science and Technology Development Agency (NSTDA) and the Ministry of Science and Technology (MOST), one of four such agencies. The guiding principle of NANOTEC is to contribute to society; increase Thailand's competitiveness; and improve the quality of life and the environment of the people of Thailand through research and development in nanoscience and nanotechnology. NANOTEC undertakes and supports research, development, design and engineering in nanotechnology, and the transfer of the resulting technology to industry and the marketplace. In 2013, the Central Laboratory of NANOTEC consisted of twelve units located at the Thailand Science Park. These covered areas including nano-cosmeceuticals (working towards products such as nano-emulsions and controlled release nano-capsules) and nano-molecular target discovery (for biomedical applications), as well as nano delivery systems, nanomaterials for energy and catalysis; hybrid nanostructure and nanocomposites; safety and risk assessment; integrated nano-systems; nanoscale simulation; functional nanomaterials and interfaces; nano characterisation; nano functional textiles; and engineering and manufacturing characterisation.

[189] https://www.mti.gov.sg/ResearchRoom/Pages/Science-and-Technology-Plan-2010.aspx
[190] www.edb.gov.sg
[191] www.ida.gov.sg
[192] www.a-star.edu.sg/
[193] www.ibn.a-star.edu.sg/
[194] www.a-star.edu.sg/imre
[195] https://www.a-star.edu.sg/ime/
[196] www.a-star.edu.sg/dsi/
[197] http://www.ibn.a-star.edu.sg/about_ibn_6.php?expandable=0
[198] http://www.nanotec.or.th/th/wp-content/uploads/2013/05/NANOTEC-brochure11.pdf

In 2012, the National Nanotechnology Policy Framework (2012-2021)[199] and the Nanosafety and Ethics Strategic Plan (2012-2016)[200] were approved by government for implementation by the Ministry of Science and Technology, and relevant agencies. The Framework has three primary goals:

- Improving agricultural technology and manufacturing industry that meet the demand of the market through nanotechnology;
- Utilising nanotechnology to develop materials, products, and equipment in order to enhance the quality of life, wellness, and environment; and
- Becoming ASEAN's leader in nanotechnology research and education.

The overall strategic direction of the Framework encompasses four target clusters, including health and medicine, and defines seven flagship products including nano-sensors for medical diagnostics, nano drug delivery systems and nano-cosmeceuticals. It aims to achieve its goals through actions in human resources, research and development, infrastructure development, management (of quality, safety and standards) and technology transfer.

The strategy in Thailand is largely to focus on product development through nanotechnology. To this end, NANOTEC is addressing national and NSTDA priorities under the Framework through ten flagship programmes to develop specific products, some of which address health concerns (e.g. a vector control system for mosquitos, and nano-biosensors for UV, heavy metals and bacteria). It is also developing platforms for drug delivery based on nano-encapsulation and molecular complexation techniques for the controlled release and target delivery of bioactive compounds. Nano-carriers studies of NANOTEC include work on self-assembly nanoparticles, polymer conjugates, nano-emulsion and molecular inclusion complexes. In addition, novel targeting moieties such as peptides, magnetic, and antibodies are being explored. In nano-molecular target discovery, the design and development of antibody fragments for targeting infectious diseases and cancer are being investigated. The emphasis is on therapeutic antibody-based nano-molecules and molecular diagnostic tests.

6.3.4 Western Asia

6.3.4.1 Israel

The first Israeli nanotechnology policy initiative was the establishment of the Israel Nanotechnology Initiative (INNI)[201] in 2002 as a shared action of the Forum for National Infrastructures for Research & Development (TELEM)[202] and the ministry for the economy (now called the Ministry for Industry, Trade and Labour)[203]. INNI's mission is "to make nanotechnology the next wave of successful industry in Israel by creating an engine for global leadership". To achieve this, actions have been taken on scientific research in nanoscience and nanotechnology (NST); on increasing public-private collaboration on NST; on speeding up commercialisation of NST; and on leveraging funding from both public and private sources to support NST in Israel. INNI is closely linked to the national system with its Director appointed by the Chief Scientist at the Ministry and the Board operating out of the MAGNET Programme[204] at the Office of the Chief Scientist.

Since NST was identified as a national priority area in 2007, the areas that have been targeted have included research infrastructure, training Israeli scientists in NST, attracting foreign researchers to work in Israeli institutions, increasing collaboration in NST and publication output of the highest international standard, fostering public-private partnerships and knowledge transfer and commercialisation of NST. Investment has been running at about USD 20 million (EUR 15.5 million[205]) per annum for basic NST equipment plus another almost USD 10 million (EUR 8 million[206]) per annum for new infrastructure and facilities.[207] The aim has been to create a sustainable basis for NST within the universities via training, recruitment and the provision of facilities on the basis that, without a

[199] http://www.nanotec.or.th/en/wp-content/uploads/2012/02/The-National-Nanotechnology-Policy-framework-exe-sum.pdf
[200] http://www.nanotec.or.th/en/
[201] http://www.nanoisrael.org/
[202] http://www.trdf.co.il/eng/fundinfo.php?id=2846
[203] http://www.economy.gov.il/English/Pages/default.aspx
[204] http://www.moital.gov.il/NR/exeres/111E3D45-56E4-4752-BD27-F544B171B19A.htm
The Magnet programme supports companies and academics to form consortia to research precompetitive generic technologies. Direct funding is up to 66% of the cost of the project with no obligation to repay royalties.
[205] Average yearly conversion rate, 2012 (*source*: www.wolframalpha.com)
[206] Average yearly conversion rate, 2012 (*source*: www.wolframalpha.com)
[207] Figures for funding under the programme to 2012.

strong research base, direct investment in technology will not be able to generate the required returns in terms of technology development and deployment.

In addition, the Triangle Donation Matching (TDM) programme[208] was launched under the INNI in 2006, a five-year national programme to support NST research infrastructure in six universities in Israel. A total of USD 250 million (EUR 198 million[209]) has been invested by Israeli Universities, private donors and the Israeli government to recruit leading nano-scientists and acquire equipment, facilities and laboratories for six nano-centres at the universities. The first impact was seen at Technion, Israel's Institute of Technology[210, 211], in 2005 (before the official launch of the programme), the other five research universities receiving support in 2006.

To help academics and industry to access the facilities of the six Israeli nano centres, the INNI has made available a national nano infrastructure catalogue[212]. The catalogue of equipment includes pricing for the use of the equipment and contact information. Industry users are supported by the university nano-centres to enable them to be effective in using their R&D equipment.

INNI also has introduced the Industry-Academia Matchmaking programme to make Israeli nanotechnology more visible to the industrial and investment communities and to promote Israel's NST research capabilities to potential partners. Experts help potential collaborators to meet, access expertise and access funding depending on their needs. They engage with key nanotechnology stakeholders in Israel and abroad, initiate and managing national and international networks in NST. They also gather statistics and market information on NST.

6.3.4.2 Saudi Arabia[213]

The King Abdul Aziz City for Science and Technology (KACST) was established in 1985 as the Kingdom's main agency for promoting research and development. In 2002, Saudi Arabia decided to build further on the work of KACST by putting in place a National Policy for Science and Technology (NPST) with plans to increase R&D funding to 1.6% of GDP. KACST was made responsible for implementing the policy which included five-year strategic plans (missions) in eleven research areas prioritising areas relevant to ICT including nanotechnology and information technology, electronics, photonics, advanced materials, as well as others: water, oil and gas, petrochemicals, biotechnology, space and aeronautics, energy and environment. The National Nanotechnology Programme (NNP) was established to deliver the plan.

During the implementation of the NNP, nanotechnology centres began to be established, such as the Centre of Excellence in Nanotechnology (CENT) established 2005 at the KFUPM[214]; and the CNT established in 2006 at the KAU[215] that covers the fields of electromechanical (MEMS/NEMS) devices, semiconductors nanomaterials and computational nanotechnology. These centres operated in the context of the multidisciplinary programme of Strategic Priorities for Nanotechnology 2008-2012, put in place by the Saudi Arabian Ministry of Economy and Planning in 2008.

Additional nanoscience and nanotechnology centres followed. The Centre of Excellence of Nano-manufacturing Applications (CENA) was established in 2009 at KACST and the King Abdullah Institute for Nanotechnology (KAIN)[216] established in 2010 at the KSU in the Riyadh Techno Valley. The KAIN in particular is focussed on medicine and pharmaceuticals as one of its main areas which also cover food and environment, energy, water treatment and desalination, telecommunications, and manufacturing and nanomaterials.

6.3.4.3 Turkey

Nanotechnology was one of eight strategic fields of research and technology identified in the Vision 2023 Technology Foresight Study prepared by the Supreme Council of Science and Technology (SCST) in 2002. The Foresight Study formed part of the development of the National Science and

[208] http://www.nanoisrael.org/category.aspx?id=1278
[209] Average yearly conversion rate, 2006 (*source*: www.wolframalpha.com)
[210] The Technion centre was co-funded by the Russel Berrie Foundation via a donation of USD 26 million which, together with funding from Technion itself, the Office of the Chief Scientist and the Ministry of Finance, made up to USD 78 million for the Russell Berrie Institute for Research in Nanotechnology.
[211] Israel Institute of Technology http://www.technion.ac.il/en/
[212] http://www.nanoisrael.org/category.aspx?id=13671
[213] A review of nanotechnology development in the Arab World, Bassam Alfeeli et al., Nanotechnology Review, 2013 (05/2013; 2(3):359-377)
[214] King Fahd University of Petroleum and Minerals, Riyadh
[215] King Abdul Aziz University, Jeddah
[216] http://nano.ksu.edu.sa/en

Technology Policies 2003-2023 Strategy Document. In nanotechnology, seven thematic priority areas were selected: (i) nano-biotechnology (ii) nano-photonics, nano-electronics, nano-magnetism; (iii) nanomaterials; (iv) fuel cells, energy; (v) nano-characterisation; (vi) nanofabrication; and (vii) nano-sized quantum information processing. Nanotechnology was also included as a priority technology field in the Development Programme prepared by State Planning Organisation (SPO) for the period 2007-2013.

Projects in nanotechnology are supported by the Scientific and Technological Research Council of Turkey (TUBITAK) and the Ministry of Development (MoD and between 2007 and 2014 it is estimated[217] that nanotechnology has received State support of about one billion Turkish Lira, or c. USD 500 million (EUR 367 million[218]). Over 20 nanotechnology research centres, departments and graduate schools have been established including NanoTam[219] at Bilkent University; Sabanci University Nanotechnology Research and Application Center (SUNUM)[220]; and the Micro and Nanotechnology Department at the Middle East Technical University[221].

6.4 Oceania

6.4.1.1 Australia

The National Nanotechnology Strategy (NNS) was put in place by the Australian Department of Innovation, Industry, Science and Research in 2007 as a dedicated strategy for nanotechnology in 2007 to 2009. The Australian Office of Nanotechnology was established to co-ordinate the strategy and ensure a whole-of-government approach to nanotechnology issues. A Public Awareness and Engagement Programme formed part of the NNS.

In 2009-2010, the NNS was replaced with a National Enabling Technology Strategy (NETS) a comprehensive national framework for the safe and responsible development of novel technologies (including nanotechnology and biotechnology). With funding over four years of AUS 38.2 million (EUR 28.3 million[222]), the strategy aimed to ensure good management and regulation of enabling technologies in order to maximise community confidence and community benefits from the commercialisation and use of new technology. Public engagement has remained an important topic in Australia for nanotechnology and other novel technologies.

In 2012, the National Nanotechnology Research Strategy[223] was prepared by the Australian Academy of Science, using funding received from the National Enabling Technologies Policy Section in the Department of Industry, Innovation, Science, Research and Tertiary Education. The Research Strategy identified nano-biotechnology and nanomedicine as national research strengths. It set out a vision for Australia to become a world leader in a nanotechnology-driven economy with a strong nanotechnology research base and the means to assist industry to revolutionise its portfolio through nanotechnology, for greater competiveness and to address the grand challenges most relevant to Australia including health, disease and ageing. The Strategy highlighted the importance of infrastructure, interdisciplinary research, international engagement, the translation of research, and the growth of SMEs.

Australia also operates a network to link research facilities across the country, the Australian Nanotechnology Network[224]. The Network was established by bringing together four seed funding networks. It comprises about 1,000 active researchers from universities, institutes and government research organisations, half of whom are students. Its aims are to promote collaboration, increase multidisciplinary awareness and collaboration, foster forums for postgraduate and early career researchers, increase and improve awareness of nanotechnology infrastructure, and promote international links.

6.4.1.2 New Zealand

Nanotechnology strategies in New Zealand began by taking a networking approach and were led by

[217] http://www.issi2015.org/files/downloads/all-papers/0720.pdf
[218] Average yearly conversion rate, 2007-2014 (*source*: www.wolframalpha.com)
[219] http://www.nanotam.bilkent.edu.tr/eng/main.html
[220] http://s-unum.sabanciuniv.edu/
[221] http://mnt.metu.edu.tr/
[222] Average yearly conversion rate, 2010-2013 (*source*: https://www.ecb.europa.eu/stats/exchange/eurofxref/html/eurofxref-graph-aud.en.html)
[223] https://www.science.org.au/publications/national-nanotechnology-research-strategy
[224] http://www.ausnano.net/index.php?page=home

the MacDiarmid Institute for Advanced Materials and Nanotechnology[225]. The Institute, formed in 2002, is a partnership between five Universities and two Crown Research Institutes in Auckland, Palmerston North, Wellington, Christchurch and Dunedin. It was awarded USD 23.2 million (EUR 19 million[226]) funding for 2003-2006 from the Ministry of Education and, in early 2006, developed a "Nanotechnology Initiative for New Zealand"[227] identifying where capability in nanotechnology could be developed in the country. The Initiative identified six programmes for nanoscience and nanotechnology research: bio-nanotechnologies; nano-photonics, nano-electronics and nano-devices; nanotechnology for energy; nano- and micro-fluidics; nanomaterials for industry; and social impacts of nanotechnology.

Also in 2006, the New Zealand government released a Nanoscience and Nanotechnologies Roadmap (2006-2015)[228]. Highlighting international and national research, the Roadmap placed nanotechnology amongst government's strategic priorities, setting high level directions for nanotechnology-related research and policy in New Zealand. Three priority areas for public funding were identified: tools and techniques; diagnostic devices; and the creation of new materials. The Ministry of Science and Innovation was in charge of policy action to implement the Roadmap.

The Ministry of Science and Innovation *Statement of Intent 2011-14* highlighted two high-level priorities – growing the economy and building a healthier environment and society. In addition to the traditional resource sectors of New Zealand, it sought to capability in knowledge-intensive activities, such as high-technology manufacturing and the services sector. Six priority areas were identified including health and society, biological sciences, energy and minerals, high-value manufacturing and services, hazards and infrastructure, and the environment[229].

6.5 Africa

6.5.1.1 South Africa

Since 2002, the Republic of South Africa has launched several national nanotechnology initiatives to strengthen national capabilities in this field. Relevant steps have included:

- In 2002, the formation of the South African Nanotechnology Initiative (SANi)[230] with membership comprising of academics, researchers, engineers, private sector companies, and research councils;
- In 2003, the launching of South Africa's Advanced Manufacturing Technology Strategy (AMTS)[231] by the Department of Science and Technology (DST);
- In 2005, the publication of the National Strategy on Nanotechnology (NSN)[232] by the DST. The strategy focuses on four areas:
  - establishing characterisation centres (national multi-user facilities);
  - creating research and innovation networks (to enhance collaboration: inter-disciplinary, national and internationally);
  - building human capacity (development of skilled personnel); and
  - setting up flagship projects (to demonstrate the benefits of nanotechnology towards enhancing the quality of life, and spurring economic growth).

South Africa launched its first nanotechnology innovation centres in 2007 at the CSIR[233] and MINTEK[234]. Each centre has developed collaborative research programme, often with other national institutions. These include programmes in designing and modelling of novel nano-structured materials, at the CSIR- National Centre for Nano-structured Materials (NCNSM)[235], and work on the application of nanotechnologies in the fields of water, health, mining and minerals at MINTEK. In health, AuTEK Biomed[236] focuses on creating gold-based chemo-therapeutics for treating diseases such as cancer, malaria and HIV and AIDS and is a collaborative project between the gold mining

[225] http://www.macdiarmid.ac.nz/
[226] Average yearly conversion rate, 2003-2006 (*source*: www.wolframalpha.com)
[227] http://www.macdiarmid.ac.nz/a-nanotechnology-initiative-for-new-zealand/
[228] http://statnano.com/strategicplans/13
[229] http://www.mbie.govt.nz/
[230] http://www.sani.org.za/
[231] http://www.esastap.org.za/download/natstrat_advmanu_mar2005.pdf
[232] http://chrtem.nmmu.ac.za/file/35e56e36b6ab3a98fac6fc0c31ee7008/dstnanotech18012006.pdf
[233] http://www.csir.co.za/
[234] http://www.nic.ac.za/
[235] http://ls-ncnsm.csir.co.za/
[236] http://www.mintek.co.za/technical-divisions/advanced-materials-amd/project-autek/

industry and MINTEK.

In addition to engaging with European researchers through Framework Programmes, South Africa has established international collaboration mechanisms which include nanotechnology with other developing countries, e.g. the India–Brazil-South Africa (IBSA) partnership[237] enables joint projects and mobility[238] between S&T departments in those countries.

The next section reports on publishing activity in health-related nanotechnology.

[237] http://www.ibsa-trilateral.org/
[238] http://www.ibsa-trilateral.org/about-ibsa/areas-of-cooperation/people-to-people

7 PUBLICATIONS IN HEALTH NANOTECHNOLOGY

7.1 Overview

Around 1.8 million publications were identified[239] from the Web of Science as being related to nanoscience and technology (NST)[240] between 2000 and 2014. Of these, almost 200,000 relate to nanotechnology and health. The numbers for the World and EU28 & EFTA (which includes here just Switzerland and Norway) are in the table below, as nanotechnology for health and as a percentage of total health publications.

Table 7-1: Annual NST publication output for health worldwide and in the EU28&EFTA, 2000-2014

Year	World	EU28 & EFTA	
	npub	npub	%
2000	4,490	1,899	42.3%
2001	4,925	2,097	42.6%
2002	5,510	2,202	40.0%
2003	6,315	2,496	39.5%
2004	7,461	2,798	37.5%
2005	8,773	3,203	36.5%
2006	9,980	3,491	35.0%
2007	11,514	3,988	34.6%
2008	13,466	4,393	32.6%
2009	15,266	4,891	32.0%
2010	17,598	5,645	32.1%
2011	19,832	6,110	30.8%
2012	21,700	6,768	31.2%
2013	24,323	7,290	30.0%
2014	26,290	7,681	29.2%
TOTAL	**197,443**	**64,952**	**32.9%**

Source: Derived from Web of Science

The number of nanotechnology health publications increased between 2000 and 2014 by a factor of four for the EU28 plus EFTA and by a factor of six for the whole World.

The Compound Annual Growth Rates (CAGR) of publications for the EU28/EFTA and for the World were calculated with the following similar results:

- EU28/EFTA: 10% CAGR
- World: 13% CAGR

The evolution over time of publications in nanotechnology for health, as well as the entire NST field (both for (i) EU28&EFTA and (ii) the World), is depicted in the figure below, indexed by year 2000 (=1). While health publications in the two regions show similar growth rates over the time period, publications in nanoscience and nanotechnology for health (shortened here to nanohealth) have had a much faster growth rate since 2000 than for health alone.

[239] http://www.vosviewer.com/Publications

[240] Search included all those publications having been produced with "nano" as a core term. The term "nanosecond" has been omitted as not being relevant to the study.

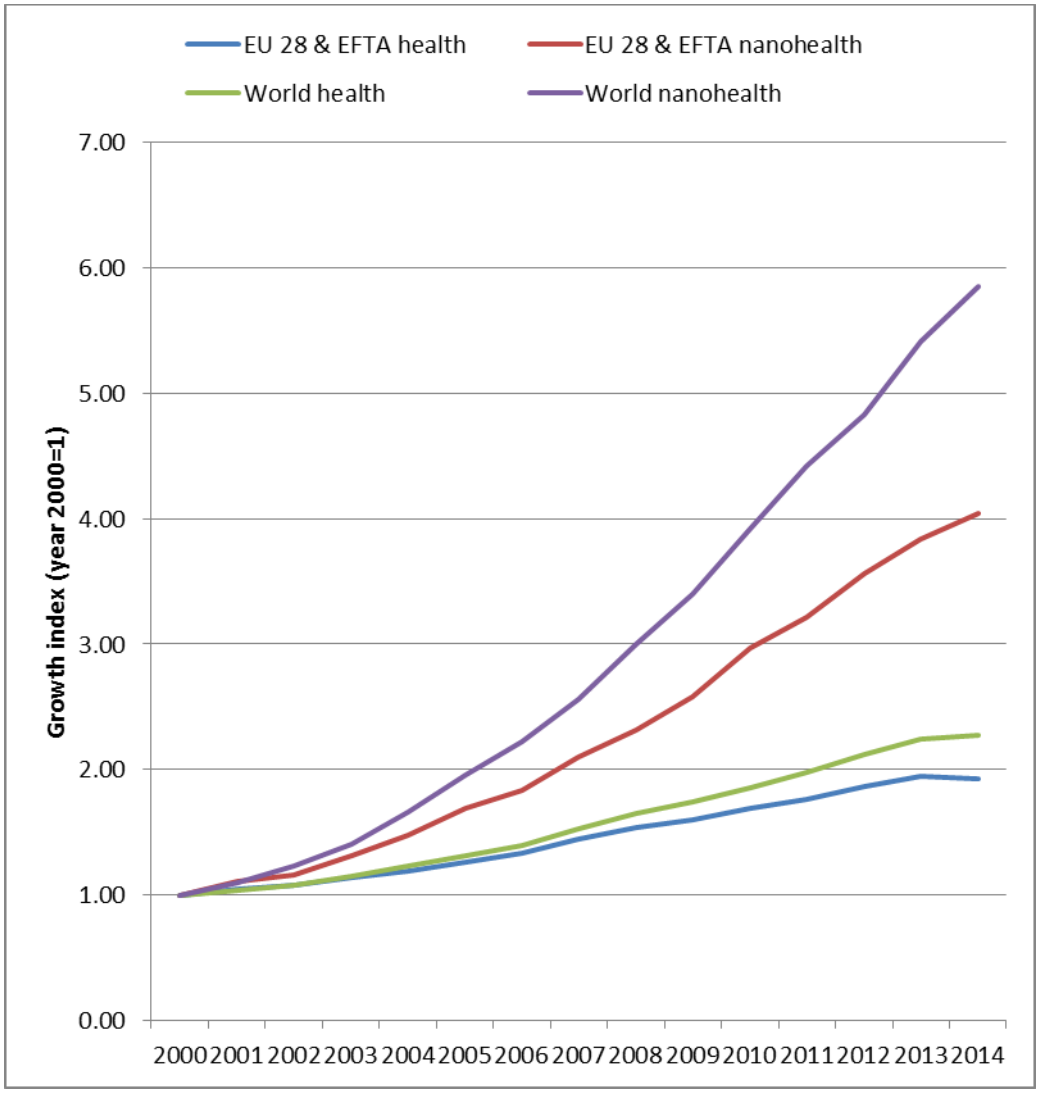


Figure 7-1: Annual NST health publication output, worldwide and EU28&EFTA, 2000-2014 (Indexed to Year 2000 = 1)

Of the c. 200,000 publications that relate to health NST in 2000-2014, 28% relate to cancer; 4 % to infectious diseases; 2% to diabetes; 5% to cardiovascular diseases; and 3% to neurodegenerative diseases. In addition, there is a 60% proportion of publications that do not fall into one of the five sub-sectors[241]. These cover topics including, for example, generic health nanotechnology research (applicable to several sectors); the use of nanotechnology in the vehicles related to healthcare; and its use in the electronic and computer-based systems that support healthcare.

The pie charts below give an indication of the proportions of publications that fall into each category, if double counting[242] is eliminated.

[241] It should be noted that publications can arise in more than one disease category (hence the figures do not sum to 100%).

[242] Double counting will arise when a publication makes reference to more than one of the health sub-sectors identified in this project e.g. cancer and cardiovascular disease.

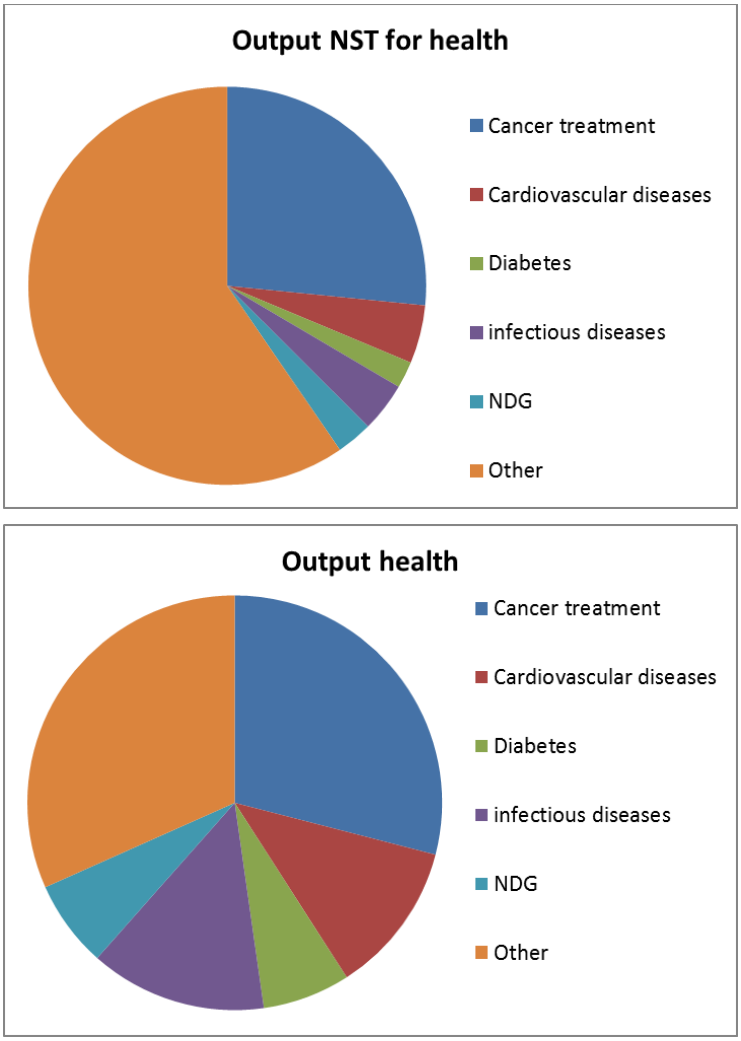


Figure 7-2: Prevalence of publications by sub-sector (i) health nanotechnology (ii) health overall
Normalised data for 2000-2014

Differences are seen in the publication proportions for health nanotechnology and health in general, as follows:

- All sub-sectors are more prevalent in all health overall than in NST health publications, although the proportion of publications for nanotechnology and cancer NST is similar to that for cancer overall.
- In NST, most research is done outside the identified sub-sectors. This is partly due to research not being specific to the sub-sectors (e.g. research related to drug delivery techniques, to medical devices and appliances and to health practices), and also, for example, research being undertaken that is not yet linked to a disease type but that may become relevant to a health sub-sector in the future.
- The proportions of NST publications for cardiovascular disease and for neurodegenerative diseases are approximately half the proportion for those diseases in health overall.
- The proportion of NST publications for diabetes is just over one third of those for diabetes in health overall; and
- The proportion of NST publications for infectious diseases is less than a quarter of the proportion in health overall.

Looking at the publications in the selected five health sub-sectors alone, 67% are on cancer-related topics, by far the highest proportion.

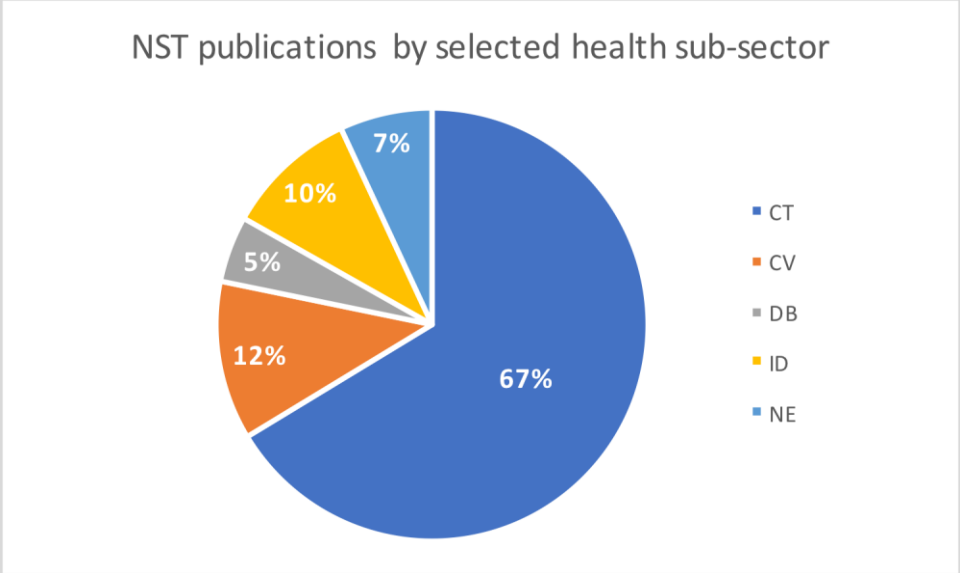


Figure 7-3: NST publications by selected health sub-sector

7.2 Activity by region and country

The most prolific region[243] for nanotechnology health publications in 2014 was Asia, followed by the EU28&EFTA and then North America (USA and Canada). The most prolific countries for nanotechnology health publications globally in 2014 were the USA and the People's Republic of China (PRC), followed by India, Germany, South Korea and Great Britain (UK) (by numbers of publications, npub). China showed a particularly strong increase, while the other countries show a normal growth of output. The distributions are presented in the figures and tables below.

Table 7-2: Most prolific regions for health nanotechnology publications, 2014

Region	npub
Asia	12,258
EU28 & EFTA	7,681
North America	6,210
Middle East	1,099
South and Central America	959
Oceania	712

[243] This is based on the data for the top 25 performing countries only.

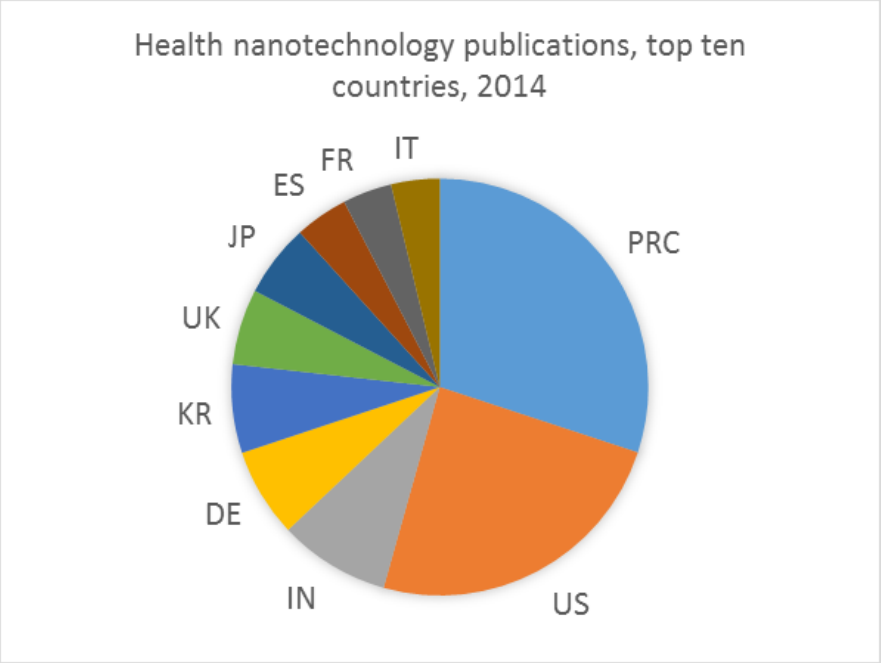


Figure 7-4: Top ten publishing countries showing their relative performance, 2014

Table 7-3: Number of health nanotechnology publications by country (top 20), 2014

Country	Region	npub
PRC (China)	Asia	6,930
USA	North America	5,590
India	Asia	1,988
Germany	EU28 & EFTA	1,591
Korea	Asia	1,583
United Kingdom[244]	EU28 & EFTA	1,353
Japan	Asia	1,302
Spain	EU28 & EFTA	950
France	EU28 & EFTA	881
Italy	EU28 & EFTA	868
Canada	North America	731
Australia	Oceania	654
Brazil	South & Central America	604
Singapore	Asia	455
Poland	EU28 & EFTA	409
Netherlands	EU28 & EFTA	404
Switzerland	EU28 & EFTA	395
Portugal	EU28 & EFTA	386
Turkey[245]	Middle East	356
Sweden	EU28 & EFTA	356

[244] The WoS database uses Great Britain but, as they include Northern Ireland, the correct term is United Kingdom.
[245] In the table for publications by region, Turkey has been included in the figures for Asia.

In the EU28, Germany and Great Britain (UK) generated the largest number of publications in 2014, followed by Spain, France and Italy (see figure below for EU28 & EFTA countries).

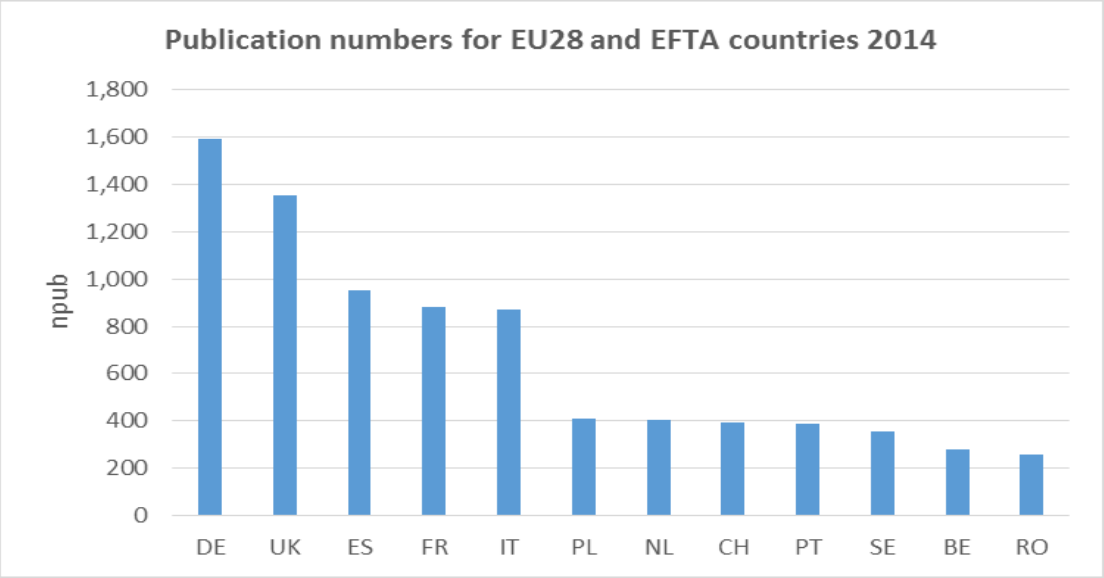


Figure 7-5: Publication numbers for EU28 and EFTA countries, 2014
Data for the top NST health publishing countries only

7.3 Activity by organisation type

Identified from the publication data, the main players in the R&D landscape of the nanotechnology for the health sector are higher education institutions, research and technology organisations and industry. The distribution of their contribution in terms of publication output differs marginally if the sector is compared to the entire NST output and if we compare the EU 28 & EFTA with the World. The most active organisations in NST for health publications in 2014 are shown in the table below. The higher education organisations with the most nanotechnology health publications globally in 2014 were the Chinese Academy of Sciences[246], Sichuan University and Harvard University as shown in the table below of the top 25 publishing organisations. To see European higher education institutions, it is necessary to look at the top fifty where only University College London (UCL), the University of Cambridge and the University of Copenhagen are present.

[246] Note that organisations such as the Chinese Academy of Sciences encompass researchers based in a large number of locations (such as universities and research institutes in China).

Table 7-4: Publications in health nanotechnology for higher education and research organisations, 2014

	Country	University/ Research Institute	npub
1	PRC	Chinese Academy of Sciences	1219
2	PRC	Sichuan University	313
3	USA	Harvard University	274
4	PRC	Shanghai Jiao Tong University	274
5	SG	National University of Singapore	247
6	PRC	Fudan University	235
7	PRC	Zhejiang University	230
8	Korea	Seoul National University	215
9	PRC	Jilin University	214
10	PRC	Nanjing University	186
11	PRC	Soochow University	183
12	PRC	Tsinghua University	181
13	USA	MIT	177
14	PRC	Peking University	176
15	Singapore	Nanyang Technology University	162
16	India	Indian Institute of Technology	160
17	PRC	Southeast University	154
18	PRC	Wuhan University	153
19	USA	University of Michigan	144
20	PRC	South China University of Technology	144

The list of the top ten European higher education institutions and other research organisations is led by University College London (UCL, UK), the University of Cambridge (UK) and the University of Copenhagen with over 100 publications, followed by Imperial College (UK), the Polish Academy of Sciences (PL), and the Universities of Ghent (NL), Manchester (UK) and Barcelona (ES). Within the top ten, four are UK institutions. In the main, these are not organisations that feature strongly in terms of funding in the Framework Programmes for nanotechnology and health (see *Activity by organisations receiving funding* in the section on *The EU Framework Programmes: Funding and participation data* in this report), Imperial College London (UK) being an exception.

Table 7-5: Publications in health nanotechnology for European HEIs and other research organisations, 2014

	University/ Research Institute	Country	npub
1	University College London	UK	120
2	University of Cambridge	UK	109
3	University of Copenhagen	DK	103
4	Imperial College London	UK	91
5	Polish Academy of Sciences	PL	89
6	University of Ghent	BE	88
7	University of Manchester	UK	87
8	University of Barcelona	ES	82
9	University of Mainz	DE	79
10	University Minho	PT	79

While publishing at a much less frequent rate, some companies are also active. The most active companies publishing in NST for health (2014) are shown in the table below. The companies with the most nanotechnology health publications globally in 2014 were AstraZeneca, Merck and Bristol Myers Squibb, as shown in the table of the top publishing companies worldwide. Comparing with the countries engaging in the Framework Programmes, FP6 and FP7, there are no companies in common, with the possible exception of IBM (here, its US operation and, in projects, its Swiss operation).

Table 7-6: Publications in health nanotechnology for the top publishing companies, 2014

Country/ Region	Company	npub
EU28 & EFTA	AstraZeneca	30
USA	Merck and Company Inc.	30
USA	Bristol Myers Squibb Co.	22
EU28 & EFTA	H Lundbeck	16
EU28 & EFTA	Novartis	13
USA	IBM Corp.	11
EU28 & EFTA	Mosa Diagnostics GmbH	11
Japan	Eisai & Co. Ltd.	10
USA	Genentech	10
EU28 & EFTA	Glaxo Smith Kline	10
USA	Pfizer	10
Japan	Shimadzu Co. Ltd	9
EU28 & EFTA	BASF SE	9

The next section looks at the patenting activity in health-related nanotechnology, over time, by country of applicant, by applicant organisation and by patents granted.

8 PATENTING IN HEALTH NANOTECHNOLOGY

8.1 Overview

This section looks at patenting activity in nanotechnology and health by patent filings and patents granted at the leading global patent offices and by country of applicant and country of inventor, and by organisation, including companies, over the time period 1999-2011.

The patents and patent families (groups of patents related to the same invention) were identified by searching using the combination of keywords (identified within the NanoData project for the sector (and sub-sector as appropriate)) and IPC (International Patent Classification) numbers. The IPC numbers used were both those for nanotechnology i.e. B82 (or B82Y for manufactured nanomaterials) and those related to the sector under consideration (health, energy, etc.)[247]. The patent family to which those patents belonged was identified and all the patents in the patent families were retrieved.

The search was made for patents registered at the USPTO (US Patent and Trademark Office), EPO (European Patent Office) and WIPO (World Intellectual Property Organisation) thereby identifying USPTO, EPO and PCT applications. PCT[248] applications registered at WIPO are protected under the Patent Cooperation Treaty (PCT), an international treaty that enables the filing of patents to protect inventions in the countries[249] that are members of the treaty.

8.2 Number and evolution over time of health nanotechnology patent families

Using the above methodology, 45,127 (simple) nanotechnology patent families[250, 251] of granted patents and patent applications were found in the period 1993-2011[252]. All these were from the European Patent Office (EPO or EP), US Patent and Trademark Office (USPTO or US) or the World Intellectual Property Organisation (WIPO)[253].

In the same period, the number of health-related patent families identified among the nanotechnology patents is 2,894, 6.4% of all nanotechnology patent families. As applications may have been filed with multiple authorities, the percentages for PCT, EP and US do not sum to 100%. The highest percentage of applications relating to health and nanotechnology is in the US (89.3%) and the lowest at the EPO (47.4%), the difference being almost a factor of two.

Table 8-1: Absolute numbers and percentages of patents on health and nanotechnology

Nanotechnology and Health Applications (1993-2011)	Absolute Number	Percentage
Total Patent Families	2,894	100%
PCT Applications	1,891	65.3%
EP Applications	1,371	47.4%
US Applications	2,583	89.3%

[247] Thus all patent documents including at least one of the keywords (in title or abstract) was found but only when the patent was classified as being related to at least one of the sectorial IPC codes.
[248] http://www.wipo.int/pct/en/
[249] By filing one international patent application under the PCT, applicants can simultaneously seek protection for an invention in 148 countries throughout the world. http://www.wipo.int/pct/en/pct_contracting_states.html
[250] The definition of simple family is used, in which all documents having exactly the same priority or combination of priorities belong to one patent family (http://www.epo.org/searching/essentials/patent-families/definitions.html). The patent families include at least one PCT, EPO or USPTO patent application.
[251] A patent family is defined by WIPO (the World Intellectual Property Organisation) as a set of patent applications inter-related by either priority claims or PCT national phase entries, normally containing the same subject matter. http://www.wipo.int/
[252] This year refers to the oldest year of the priority patents.
[253] While patents can be filed in individual patent offices, many inventors choose to file applications under the Patent Classification Treaty (PCT). All WIPO applications are PCT applications.

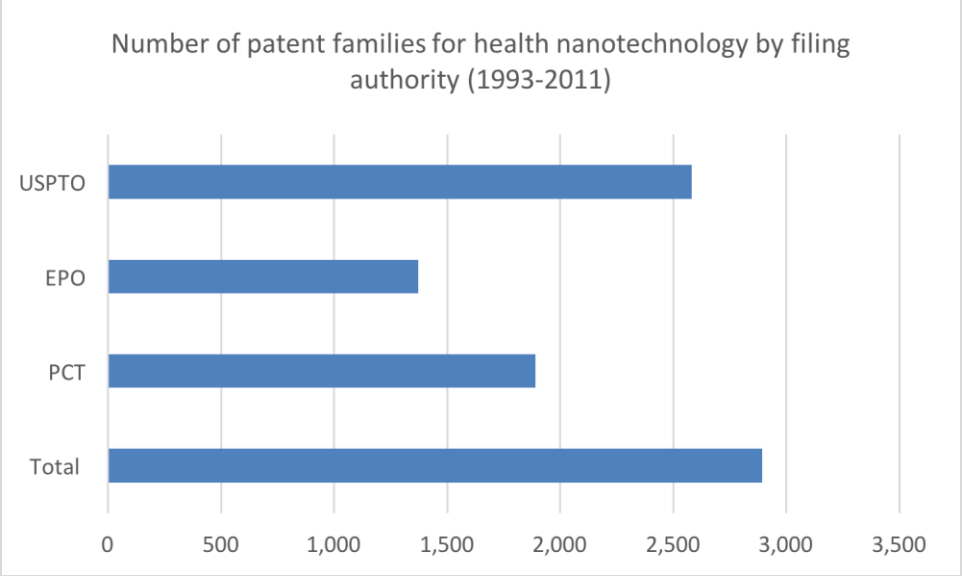


Figure 8-1: Number of patent families by filing authority (PCT, EPO, and USPTO)

The figure below shows the evolution over time of patent applications to WIPO (PCT), the EPO or USPTO as measured by the percentage of patent families.

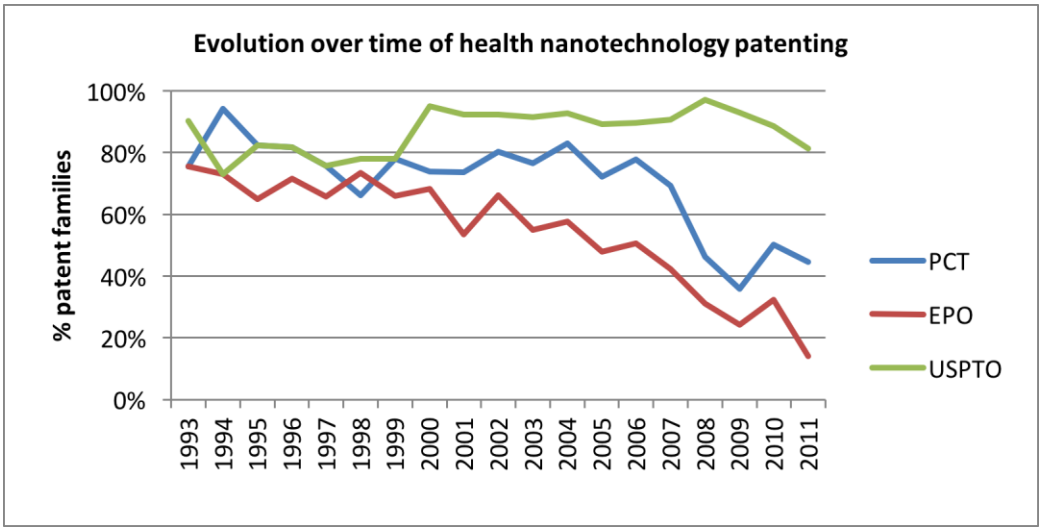


Figure 8-2: Evolution over time of WIPO (PCT), EPO and USPTO health nanotechnology patenting

The percentage of health nanotechnology patent applications in the EPO and for PCTs has dropped significantly over time, while the percentage has been more stable for USPTO filings[254]. This trend may indicate that patent filing in the US has remained important while the importance of filing in Europe or as a PCT has decreased. It may also reflect the fact that the majority of patentees are from the US, as indicated in the following sections. The trend supports the concept that patenting in the US has become relatively more important over time than patenting at EPO or as a PCT.

[254] It should be noted that the cost of applying for a US patent for an extended market is low compared with an EPO patent. There is less scrutiny of a US patent and there is evidence that a higher proportion of US patents are granted for inventions that are not novel, resulting in litigation later.

8.3 Activity by filing country and region

By looking at PCT applications, it is possible to obtain an indication of the relative patenting activity of countries and regions. The top ten patent authorities through which PCT applications were filed are shown in the table, the US being by far the most prolific, followed by Europe (EPO), Japan and the UK. The sum of the figures for the European patent offices in this top ten table and the EPO is just 362, considerably less than in the US. Even if all the remaining EU countries are allocated the figure of the lowest European country in the table (Germany, 22), the total for the EU28 plus the EPO is less than the US.

Table 8-2: Number of nanotechnology health patent families by PCT receiving authority

Receiving Authority	No. of Patent Families (1993-2011)
United States	1021
European Patent Office (EPO)	208
Japan	98
United Kingdom	94
International Bureau (WIPO)	85
South Korea	48
Canada	40
France	38
China	35
Germany	22

8.4 Activity by country of applicant

PATENT APPLICATIONS

Within the group of 2,894 health-related nanotechnology patent families, there is at least one EU28 or EFTA applicant in less than 30% of them while there is participation from the rest of the world in over 75% of cases.

Table 8-3: Origin of patent applicants, EU/EFTA and Rest of World (1993-2011)

	EU28 & EFTA	Rest of World
Number of health nanotechnology patent families	835	2,213
Percentage of health nanotechnology patent families	28.8%	76.4%

Applicants may file patents with more than one patent authority, e.g. at the USPTO and as a PCT. The table below shows the data for the top 25 countries of applicants, as well as indicating the percentage of patent families for each. EU28 and EFTA countries are marked in bold. As patents may be filed with more than one authority (including PCT, US and EP applications), the percentages can sum to more than 100%.

By far the highest number of patent families is found where the country of the applicant is the US. Germany and the UK have the next highest number of applicants, followed by Japan. In terms of applicants from Europe, Germany and the UK are followed by France, Switzerland, the Netherlands, Italy and Spain, all with over 60 patent families. For Asia, the lead country for applicants, Japan (136), is followed by Korea (106), China (67), India (61), Taiwan (Chinese Taipei, 45) and Singapore (21). The only South American country applicants that feature are from Brazil (24).

Table 8-4: Patent families by country of applicant, numbers and percentages (1993-2011)

	Country of applicant	No. of Patent Families	PCT	US	EP
1	United States	1625	66%	80%	38%
2	**Germany**	228	69%	57%	59%
3	**United Kingdom**	142	80%	49%	51%
4	Japan	136	80%	58%	49%
5	**France**	125	60%	69%	60%
6	Canada	113	52%	81%	27%
7	Korea	106	50%	70%	25%
8	Switzerland	87	57%	54%	41%
9	**Netherlands**	72	71%	54%	65%
10	Israel	68	56%	78%	31%
11	China	67	66%	64%	22%
12	India	61	66%	66%	31%
13	**Italy**	61	75%	49%	51%
14	**Spain**	61	74%	51%	43%
15	Taiwan (Chinese Taipei)	45	0%	98%	0%
16	**Belgium**	35	77%	77%	49%
17	**Sweden**	35	69%	49%	51%
18	Australia	32	75%	59%	41%
19	**Denmark**	31	71%	55%	45%
20	**Ireland**	26	46%	31%	65%
21	Russian Federation	25	72%	44%	12%
22	Brazil	24	75%	58%	38%
23	Singapore	21	62%	71%	24%
24	**Hungary**	21	57%	43%	29%
25	South Africa	18	78%	33%	22%

80% of patents of US applicants are filed with the USPTO while 66% are filed as PCTs. Only 38% are filed by US applicants at the EPO.

European applicants file more as PCTs than at either the EPO or USPTO. One explanation for this is that filing as a PCT provides applicants with more time to evaluate their invention and develop their patent before applying for a patent to be granted[255]. For example, 80% of patents have been filed as PCT by UK applicants in the 1993-2011 period for health nanotechnology inventions. This compares with UK applicants filing 49% at the USPTO and 51% at the EPO. The table indicates that, unlike the other Europeans, French applicants file more frequently with the USPTO than with the EPO.

[255] In most cases, there are 30 months from the filing date of the initial patent application before an applicant has to begin national phase procedures with individual patent offices. http://www.wipo.int/pct/en/faqs/faqs.html

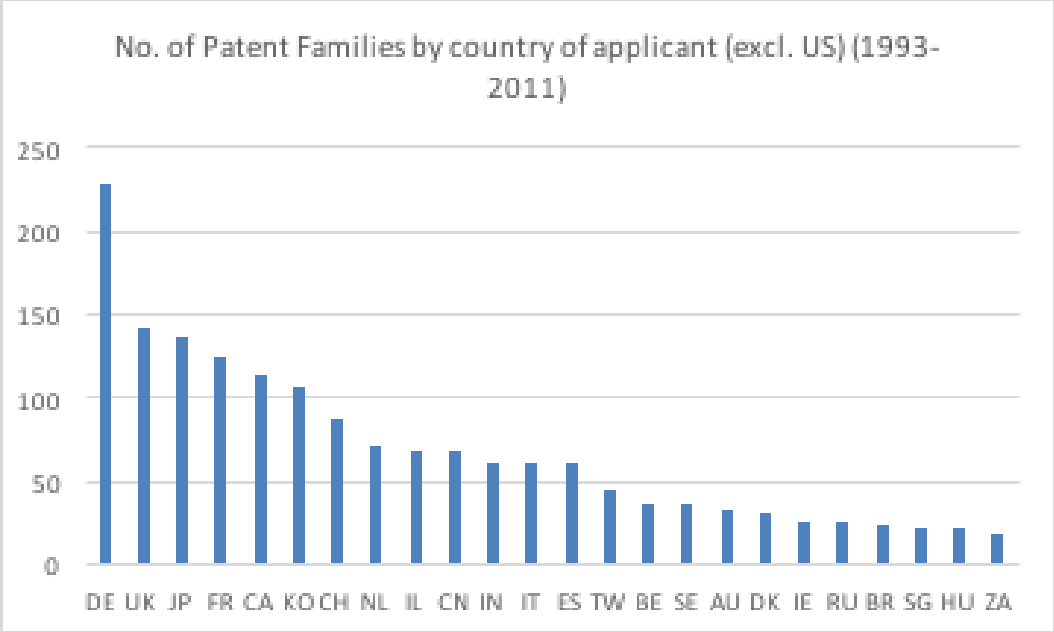


Figure 8-3: Number of patent families by country of applicant (excluding the US)

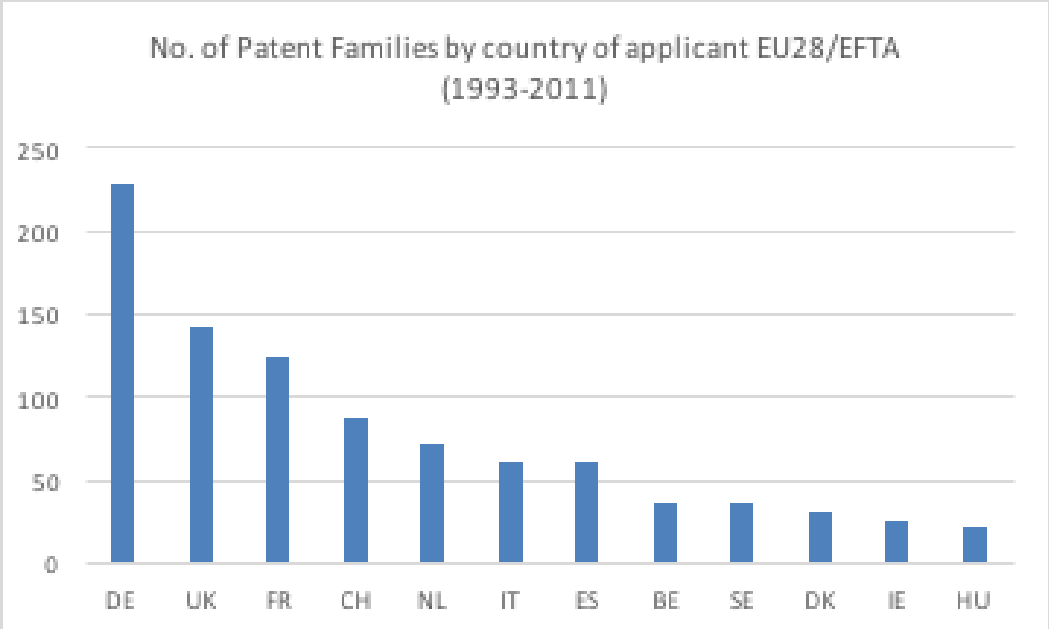


Figure 8-4: Number of patent families by country of applicant EU28/EFTA

Table 8-5: Patent families by country of applicant for EU28/EFTA (1993-2011)

World ranking	Country of Applicant	No. of Patent Families	PCT	US	EP
2	Germany	228	69%	57%	59%
3	United Kingdom	142	80%	49%	51%
5	France	125	60%	69%	60%
8	Switzerland	87	57%	54%	41%
9	Netherlands	72	71%	54%	65%
13	Italy	61	75%	49%	51%
14	Spain	61	74%	51%	43%
16	Belgium	35	77%	77%	49%
17	Sweden	35	69%	49%	51%
19	Denmark	31	71%	55%	45%
20	Ireland	26	46%	31%	65%
24	Hungary	21	57%	43%	29%

Looking at the non-EU/EFTA and non-US countries of applicants, the filing patterns are variable with Japan, Australia, the Russian Federation, Brazil and South Africa filing most as PCTs while there is a preference for USPTO filings amongst applicants from Canada, Korea, Israel and Singapore. Taiwan is not a member of the PCT so all applicants file at the USPTO. The figures for applicants from China and India show almost the same preference for PCT and USPTO filings.

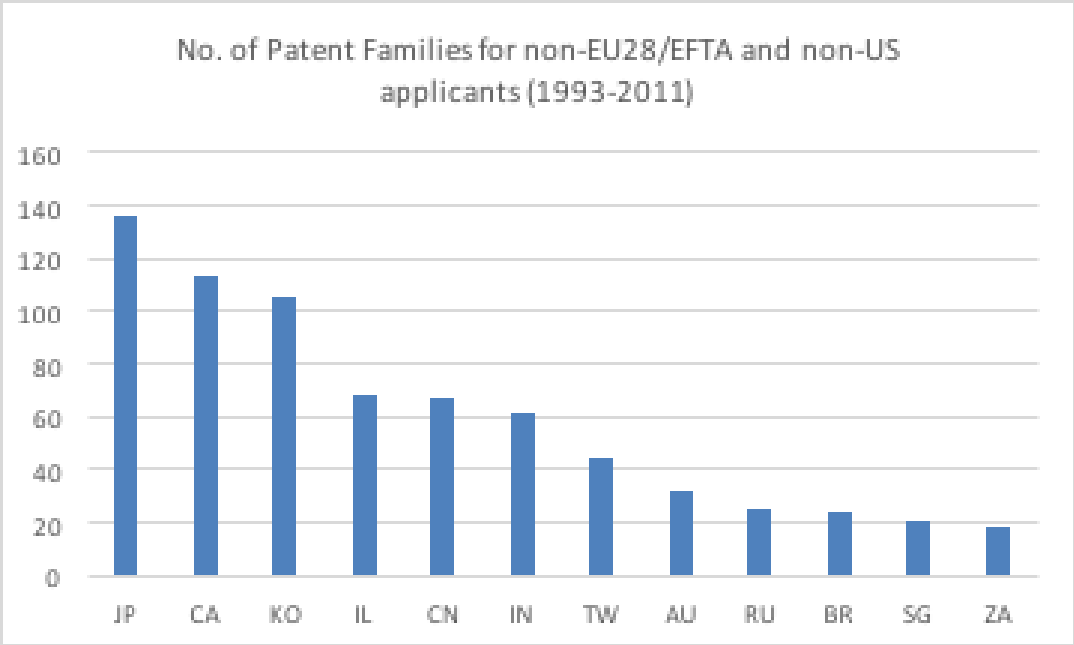


Figure 8-5: Number of patent families by country of applicant for non-EU28/EFTA, non-US

GRANTED PATENTS

Applicants from the same EU and EFTA countries perform strongly in patents granted, namely those from Germany, France and the UK.

Table 8-6: Country of applicant and number of patents granted at EPO and USPTO

	Country of applicant	No. of Patents Granted (1993-2011)	
		EPO	USPTO
1	Germany	55	39
2	France	40	29
3	United Kingdom	30	31
4	Italy	20	18
5	Netherlands	14	14
6	Switzerland	13	17
7	Spain	12	11
8	Sweden	8	13
9	Belgium	8	11
10	Ireland	8	6
11	Denmark	5	5
12	Austria	5	3
13	Finland	5	2
14	Hungary	4	3
15	Slovenia	2	2

While applicants from Germany and France have more patents granted by the EPO than the USPTO (see red bars in figure below), UK applicants have slightly more US patents than EPO ones. Swiss, Spanish and Belgian applicants also have more US than EPO patents.

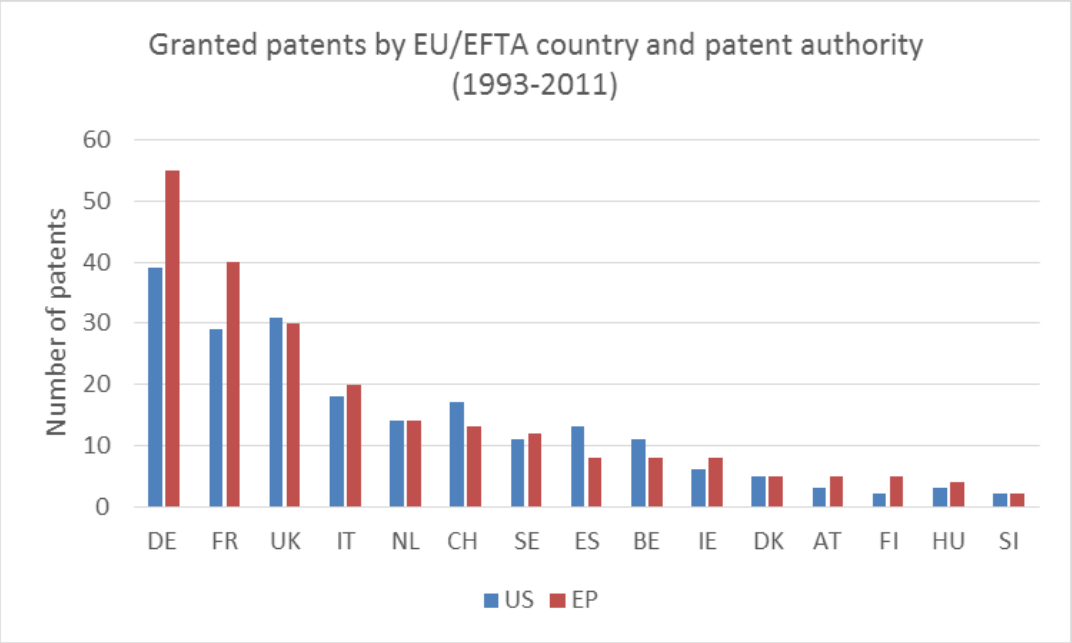


Figure 8-6: Granted patents by country of applicant for EU28/EFTA

The top eleven countries by number of applications are the same as the top eleven countries by patents granted to applicants for EU and EFTA countries, as shown in the tables below.

Table 8-7: Comparison of patent filings and patents granted by country of applicant (1993-2011)

	Country of Applicant	No. of Patent Families
1	DE	228
2	UK	142
3	FR	125
4	CH	87
5	NL	72
6	IT	61
7	ES	61
8	BE	35
9	SE	35
10	DK	31
11	IE	26

	Country of Applicant	No. of Patents Granted
1	DE	94
2	FR	69
3	UK	61
4	IT	38
5	CH	30
6	NL	28
7	SE	23
8	ES	21
9	BE	19
10	IE	14
11	DK	10

A very approximate estimate can be made of relative success in patenting between countries of applicants by comparing the number of patent families and the number of patents granted[256]. This shows a high success rate for Sweden and Italy (but perhaps the most meaningful figure is for France as it has a high number of both applications and granted patents).

Table 8-8: Estimate of relative patenting success by country of applicant

	Country of Applicant	Granted/ Applied %
1	Sweden	66
2	Italy	62
3	France	55
4	Belgium	54
5	Ireland	54
6	United Kingdom	43
7	Germany	41
8	Netherlands	39
9	Switzerland	34
10	Spain	34

When considering the country of applicant and the country of inventor as seen in patent family data, it is clear that inventions are most often patented in the country in which they are invented (see table below). However, it is not uncommon to have inventions that are patented outside of the country in which they originate. There may be some correlation with language as seen in the patenting of Swiss inventions in both France and Germany. In addition, inventions from inventors in the US are patented elsewhere and patent applications in the US may originate from work done elsewhere.

[256] It should be noted that the data do not apply to the same filings as the patents applied for in 1993-2011 will not be the same as the patents granted in 1993-2011, albeit that some overlap can be expected.

Table 8-9: Country of applicant and country of inventor table for cross-comparison

APPL	US	CA	DE	UK	IL	KR	CN	JP	CH	FR
INV										
US	1563	37	34	29	25	19	18	17	16	16
CA	45	101	2	3	2	2	2	0	0	0
CH	28	4	20	1	1	2	1	0	51	11
DE	26	2	220	4	3	1	0	4	15	2
UK	25	3	3	116	1	0	2	0	3	7
KR	20	2	2	0	0	105	2	0	0	0
CN	16	1	0	0	1	1	66	1	0	0
JP	16	0	1	0	0	0	1	133	0	1
IL	15	2	3	0	67	0	1	0	0	1
NL	14	0	13	5	0	0	1	0	3	5

8.5 Patenting activity by organisation type

8.5.1 Universities and public research organisations

PATENT APPLICATIONS

Of the top ten universities and public research organisations (PROs) with the highest number of patent families (with percentages for PCT, US and EP applications), nine are in the United States. France is the only EU28 country that features in the table, marked in bold.

Looking at the top 25 performing universities and PROs for patent families, seven out of 25 are from outside the US, just two being from the EU28 or EFTA (CNRS, France, and CSIC, Spain). The tables below show the top ten universities and PROs by number of patent families, followed by the top non-US universities and PROs (based on top 25 universities and PROs, see full table in the Annex).

Table 8-10: Number of patent families for top ten universities and PROs (1993-2011)

	Country	Organisation	No. of Patent Families	PCT	US	EP
1	US	University of California	58	63.8%	79.3%	32.8%
2	US	MIT[257]	41	82.9%	75.6%	39.0%
3	US	University of Texas	22	4.5%	81.8%	40.9%
4	US	North-western University	18	72.2%	77.8%	11.1%
5	US	University of Michigan	18	50.0%	72.2%	38.9%
6	US	Johns Hopkins University	16	37.5%	75.0%	37.5%
7	US	Emory University	16	87.5%	68.8%	50.0%
8	US	Rice University	14	78.6%	50.0%	14.3%
9	US	General Hospital Corp	14	85.7%	64.3%	21.4%
10	FR	CNRS[258]	14	64.3%	57.1%	64.3%

[257] Massachusetts Institute of Technology, US
[258] Centre National de la Recherche Scientifique, France

Table 8-11: Number of patent families in the top 25 non-US universities and PROs (1993-2011)

Rank	Country	Organisation	No. of Patent Families	PCT	US	EP
10	**FR**	CNRS	14	64.3%	57.1%	64.3%
17	JP	Japanese S&T Agency[259]	19	68.4%	31.6%	42.1%
18	BR	Uni. Fed. Minas Gerais	9	66.7%	0.0%	22.2%
19	SG	Agency for Science Technology & Research	9	66.7%	44.4%	44.4%
20	IL	Ramot at Tel Aviv University Ltd	8	75.0%	75.0%	50.0%
21	IL	Technion R&D Foundation Ltd	8	25.0%	100.0%	25.0%
25	**ES**	CSIC	8	50%	37.5%	50.0%

The table below shows the top 20 performing universities and PROs for patent families in EU28/EFTA countries. The Spanish organisation ranked 8 and 9 has been left with two separate entries to illustrate that universities (and others) may patent as PCT, at US and/or EP but also apply for patents separately at national level. These have appeared separately in the database search due to name difference. French organisations perform strongly (3 of the top 6 organisations in the table), as do Spanish organisations (6 of the top ten). Four German organisations appear in the lower half of the top 20 table. Spain in particular is represented seven times in the table with a total of 36 patent families, compared with the three French organisations together having 27 patent families.

Table 8-12: Number of patent families in the top 20 EU28/EFTA universities and PROs (1993-2011)

Rank	Country	Organisation	No. of Patent Families	PCT	US	EP
1	FR	CNRS[260]	14	64.3%	57.10%	64.3%
2	ES	CSIC[261]	8	50%	37.5%	50.0%
3	ES	Universidade de Santiago de Compostela	7	100%	28.6%	28.6%
4	FR	INSERM	7	14.3%	42.9%	42.9%
5	UK	Isis Innovation Ltd	6	100%	50%	66.7%
6	FR	CEA[262]	6	50%	16.7%	33.3%
7	ES	Universidad de Granada	5	100%	20.0%	20.0%
8	ES	Universidad de Sevilla	5	60%	100%	60%
9	ES	Universidad de Sevilla Vicerrectorado de Investigacion[263]	5[264]	0%	0%	0%

[259] The Japanese S&T Agency (JST) was formed in October 2003 as a successor of the Japanese S&T Corporation which was itself a merger in 1996 of the Japan Information Centre of Science and Technology (JICST founded 1957) and the Research Development Corporation of Japan (JRDC, founded 1961). These figures incorporate data for both the JST Agency and the JST Corporation. http://erawatch.jrc.ec.europa.eu/erawatch/opencms/information/country_pages/jp/organisation/organisation_mig_0008

[260] Centre National de la Recherche Scientifique

[261] Consejo Superior de Investigaciones Cientificas, the Spanish National Research Council www.csic.es

[262] Commissariat à l'Énergie Atomique et aux Énergies Alternatives, the French Alternative Energies and Atomic Energy Commission www.cea.fr

[263] The Spanish organisation ranked 8 and 9 have been left separate to illustrate that universities (and others) may patent as PCT, at US and/or EP but also apply for patents separately at national level. These have appeared separately in the database search due to name difference.

[264] The patents were filed at the Spanish patent office so zero percentages for PCT, EP or US are shown.

Rank	Country	Organisation	No. of Patent Families	PCT	US	EP
10	ES	Instituto Cientifico y Tecnologico de Navarra Sa	3	100%	0%	66.7%
11	ES	Institucio Catalana de Recerca I Estudis Avancats	3	66.7%	33.3%	66.7%
12	DE	Philipps Universitaet Marburg	3	66.7%	0%	0%
13	NL	Universiteit Utrecht Holding Bv	3	66.7%	0%	33.3%
14	BE	Vrije Universiteit Brussel (VUB)	3	33.3%	66.7%	0%
15	DE	Fraunhofer Gesellschaft	3	0%	0%	100%
16	CH	Universitat Zurich	3	0%	100%	33.3%
17	CH	ETH Zurich	3	0%	66.7%	100%
18	DE	Charite Universitaetsmedizin Berlin	2	100%	0%	0%
19	SI	Kemijski Institut	2	100%	0%	50%
20	DE	KTB Tumorforschungsgesellschaft	2	100%	50%	100%

GRANTED PATENTS

Of the top 15 universities and research organisations, 5 are from the EU28/EFTA countries as shown in the table below which is ranked by the highest number of EPO patents granted between 1993 and 2011. Seven of the organisations are from the US.

Table 8-13: Universities/research organisations granted patents, by EPO patent numbers

Rank	Country	Organisation	EP	US
1	US	University of California	3	18
2	US	Scripps Research Institute	3	4
3	**FR**	CNRS	3	4
4	US	University of Louisville Research Foundation Inc.	3	3
5	**ES**	Consejo Superior De Investigaciones Cientificas (CSIC)	3	1
6	US	MIT	2	15
7	JP	Japanese S&T Agency	2	3
8	US	Johns Hopkins University	2	3
9	**CH**	ETH Zurich	2	2
10	IN	Council of Scientific & Industrial Research	2	1
11	US	Mayo Foundation	2	1
12	UK	University of Strathclyde	2	1
13	**IT**	University of Rome Sapienza	2	0
14	**UK**	University of Glasgow	2	0
15	US	University of Texas	1	7

Ranking by the number of USPTO patents granted between 1993 and 2011, 12 of the top 15 universities and research organisations are in the US with just 2 in the EU28/EFTA (CNRS, France and the University of Seville, Spain).

Table 8-14: Universities / research organisations granted patents, by USPTO patent numbers

Rank	Country	Organisation	US	EP
1	US	University of California	18	3
2	US	MIT	15	2
3	US	University of Texas	7	1
4	US	University of Michigan	7	1
5	US	Stanford University	6	1
6	US	California Institute of Technology	5	1
7	US	Emory University	5	1
8	US	Northwestern University	5	1
9	US	University of Illinois	5	1
10	US	University of Florida Research Foundation Inc.	5	1
11	**ES**	Universidad de Sevilla	5	1
12	TN	Industrial Tech Research Institute	5	0
13	US	Scripps Research Institute	4	3
14	**FR**	CNRS	4	3
15	US	New York University	4	1

8.5.2 Activity of companies

PATENT APPLICATIONS

Of the top ten companies with the highest number of patent families (with percentages for PCT, US and EP applications), seven are in the United States. The Netherlands, France and Germany are the three EU28 countries that feature in the table, marked in bold. It should be noted that some may be holding companies rather than research companies or manufacturers.

Looking at the top 25 performing companies for patent families, 13 out of 25 are from outside the US, 11 of those being from the EU28 or EFTA, predominantly the Netherlands, Germany and France. The tables below show the top ten companies by number of patent families, followed by the top non-US companies (based on top 25 companies, see full table in the Annex).

Table 8-15: Number of patent families for top ten companies (1993-2011)

	Country	Company	No. of Patent Families	PCT	US	EP
1	US	Immunomedics Inc.	50	64%	88%	60%
2	US	IBC Pharmaceuticals Inc.	20	20%	95%	20%
3	**NL**	Kon Philips Elects NV	20	90%	60%	90%
4	**FR**	L'Oreal	16	13%	31%	100%
5	US	Nanosystems Llc.	16	88%	25%	19%
6	US	Neorx Corp.	12	92%	42%	50%
7	BB[265]	Boston Scientific Ltd.	11	64%	73%	27%
8	US	Boston Scientific Scimed.[266]	11	36%	0%	100%
9	**DE**	Schering AG	11	91%	36%	73%
10=	**NL**	Farmarc NL BV	10	60%	40%	60%
10=	US	Pfizer Inc.	10	50%	60%	50%

[265] Barbados

[266] In the late 1990s, Boston Scientific was reorganised into six divisions with Boston Scientific Scimed Inc. being its primary cardiology unit, still in existence today.

Table 8-16: Number of patent families for top ten non-US companies (1993-2011)

	Country	Company	No. of Patent Families	PCT	US	EP
3	**NL**	Kon Philips Elects NV	20	90%	60%	90%
4	**FR**	L'Oreal	16	13%	31%	100%
7	BB	Boston Scientific Ltd	11	36%	0%	100%
9	**DE**	Schering AG	11	91%	36%	73%
10	**NL**	Farmarc NL BV	10	60%	40%	60%
12	**IE**	Elan Pharma Int. Ltd	9	22%	33%	100%
17	**DE**	Siemens AG	8	13%	13%	13%
18	**FR**	Guerbet	8	100%	50%	88%
19	**DE**	Philips IP & Standards	8	100%	0%	100%
20	**DE**	Bayer Schering Pharma	7	57%	29%	57%
22	**DE**	Hexal AG	7	71%	29%	100%
23	**CH**	Novartis AG	7	29%	57%	57%
24	JP	Ono Pharma Co Ltd	7	71%	71%	86%

GRANTED PATENTS

The top ten companies that have been granted patents by the EPO and/or USPTO are shown in the tables below[267]. The first table shows the top ten when the figures are sorted to obtain the highest number of EPO patents and the second shows the top ten when they are sorted for USPTO patents. It is interesting to note that Immunomedics (a US company) has the highest number of granted patents from both the USPTO and the EPO. That company also appears at the top of the list above of patent applications. Only four companies are in the top ten for grantings from both the EPO and USPTO, including two from Europe: L'Oreal (France) and Chiesi Farma (Italy). Boston Scientific appears in both tables related to grantings but with different offices, one with patents granted in the US and the other with patents granted at the EPO[268, 269].

Table 8-17: Companies granted USPTO and EPO patents (sorted by EPO patents)

Country	Company	EP	US
US	Immunomedics Inc.	16	34
FR	L'Oreal	16	4
BB	Boston Scientific Ltd	7	0
IE	Elan Pharma Int. Ltd	6	3
DE	Hexal AG	6	2
US	Pfizer Inc.	5	5
IT	Chiesi Farma Spa	5	4
UK	Cancer Research Campaign Tech Ltd	4	3
FR	Guerbet	4	2
UK	Cancer Research Tech Ltd	4	2

[267] This data does not take account of there being multiple offices of one company. Where the name differs in the database, the companies are taken as being different.
[268] There is no evidence that this is a policy of Boston Scientific.
[269] There are other companies that appear more than once with similar names in the database that are branches of the same company. There was no other case identified in which a company appeared to patent from one location via the USPTO and from another via the EPO. Where there was some indication that this could be happening, the numbers of patents were too small to make a determination.

Table 8-18: USPTO and EPO granted patents by company (sorted by US patents)

Country	Company	US	EP
US	Immunomedics Inc.	34	16
US	IBC Pharmaceuticals Inc.	13	0
US	Procter & Gamble Co.	7	2
US	Nano Systems LLC	7	0
US	Theravance Inc.	6	3
CA	Nucryst Pharmaceuticals Corp.	6	1
US	Pfizer Inc.	5	5
US	Boston Scientific Scimed Inc.	5	0
FR	L'Oreal	4	16
IT	Chiesi Farma Spa	4	5

Comparing the data for patents (applied for and granted) with that for Framework Programme participation and for publishing, there is greater commonality between the universities and research organisations patenting and those engaging in Framework Programmes (e.g. CNRS, CSIC, CEA, Fraunhofer and ETHZ as well as the University of Oxford (here represented by its subsidiary Isis Innovation)) than between these and those engaging in publishing within the top ranks (where there are no organisations in common, as measured here).

For companies, it is only Pfizer that is seen as patenting as well as publishing here, and none is engaged in the top group for both patenting and Framework Programme funding.

8.6 Health and nanotechnology patents by disease type

The number of patent families in 1993-2011 was by far the highest for cancer with almost 700, the other four sub-sectors having less than 200 each. The least patented were neurodegenerative diseases (48) and diabetes (39).

Table 8-19: Number of patent families by disease type

Disease Type	No. of Patent Families (1993-2011)
Cancer	692
Infectious Diseases	154
Cardiovascular Disease	142
Neurodegenerative Diseases	48
Diabetes	39
Other	1910

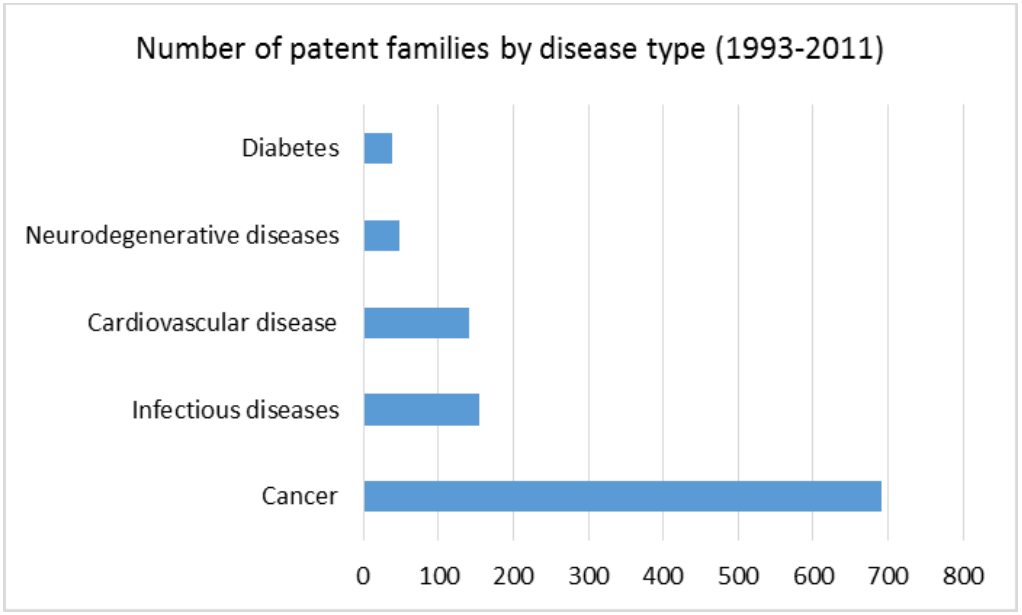


Figure 8-7: Number of patent families by disease type for five sub-sectors

The next section looks at the position of industry for health manufacturing including employment, turnover and value added and relates the information to health nanotechnology manufacturing.

9 INDUSTRY AND NANOTECHNOLOGY FOR HEALTH

As a proxy for the nanotechnology health industry, this section initially presents secondary data on the sectors of manufacturing industry for health applications in which nanotechnology is most commonly found. While not specific to nanotechnology, it indicates the enormity of the sector, one in which nanotechnology is commonly used, in terms of the number of enterprises, turnover[270], production value[271] and value added[272], and employment numbers as well as expenditure on research and development and financing through private equity.

Later in the section, secondary information is presented about the location and type of nanotechnology health companies, together with derived estimates of the value added and employment in the health nanotechnology industry in Europe. This is then related to the role of industry in nanotechnology for health.

9.1 Overview of the health industry

The manufacturing industry for health applications includes:

- Pharmaceuticals: pharmaceutical manufacturing, encompassing basic pharmaceutical products and pharmaceutical preparations (NACE C21);
- Specialised equipment: manufacturing of irradation, electromedical and electrotherapeutical equipment (NACE 26.6); and
- Instruments and supplies: manufacturing of medical and dental instruments and supplies (NACE 32.5).

It is assumed that, in large part, companies involved in these specific health industry sub-sectors will have some involvement in nanotechnology. *While only a small proportion will be specific to nanotechnology,* it is worth considering the global figures for this industry.

9.1.1 Number of EU health manufacturing enterprises

In 2013, a total of 77,500 firms were active in these manufacturing sectors, of which most (92%) were active in the manufacture of medical and dental instruments and supplies. The table below shows the number of enterprises for the above three types of health manufacturers[273].

Table 9-1: Number of EU manufacturing enterprises involved in nanotechnology for health[274]

	2005	2006	2007	2008	2009	2010	2011	2012	2013
Pharmaceuticals	4,169	4,000	:	3,977	4,606	4,000	4,000	4,000	4,400
Specialised equipment	:	:	:	:	2,092	2,124	2,010	2,039	2,100
Instruments and supplies	:	:	:	60,000	60,000	62,353	63,322	63,100	71,000
Total	4,169	4,000	0	63,977	66,698	68,477	69,332	69,139	77,500

Note: 2005 – 2011: EU-27; 2012-2014: EU-28
Source: Eurostat, Annual detailed enterprise statistics for industry (NACE Rev. 2, B-E)

9.1.2 Turnover, production and value-added in EU health manufacturing

The pharmaceuticals industry consists of a relatively small number of very large, capital-intensive enterprises. In 2005-2013, it generated the highest turnover and production value, as well as value-added, of the three sectors (see table below) while having approximately 5% of the total number of health product manufacturing companies.

[270] Turnover is defined in these statistics as market sales of goods or services supplied to third parties (Source: Eurostat).
[271] Production value measures the amount actually produced by the unit, based on sales, including changes in stocks and the resale of goods and services (Source: Eurostat).
[272] Value added is the gross income from operating activities after adjusting for operating subsidies and indirect taxes. Value adjustments (such as depreciation) are not subtracted (Source: Eurostat).
[273] EUROSTAT (2015) Annual detailed enterprise statistics for industry (NACE Rev. 2, B-E)
[274] 2005 – 2011: EU-27; 2012-2013: EU-28

Table 9-2: Turnover, production value and value added of EU manufacturing enterprises involved in nanotechnology for health

Manufacturing	2005	2006	2007	2008	2009	2010	2011	2012	2013
Turnover in EUR million									
Pharmaceuticals	170,188	186,218	201,376	209,787	217,042	231,191	231,939	227,879	263,771
Specialised Equipment	-	-	-	12,150	13,748	-	-	-	18,784
Instruments and Supplies	-	-	-	61,869	57,155	59,000	62,565	63,384	71,000
Total	170,188	186,218	201,376	283,806	287,945	290,191	294,504	291,263	353,554
Production value in EUR million									
Pharmaceuticals	161,148	177,035	192,988	193,714	200,000	213,269	209,366	208,566	231,178
Specialised Equipment	-	-	-	11,005	-	-	-	-	18,016
Instruments and Supplies	-	-	-	56,226	52,673	-	56,033	56,413	63,000
Total	161,148	177,035	192,988	260,945	252,673	213,269	265,399	264,979	312,194
Value added in EUR million									
Pharmaceuticals	59,044	68,324	71,175	76,436	-	85,872	85,845	83,807	-
Specialised Equipment	-	-	-	4,030	4,328	-	-	4,887	-
Instruments and Supplies	-	-	-	24,983	24,026	25,000	26,874	26,530	-
Total	59,044	68,324	71,175	105,450	28,355	110,872	112,719	115,225	

Source: Eurostat, Annual detailed enterprise statistics for industry (NACE Rev. 2, B-E)

9.1.3 Employment in EU ICT manufacturing

In 2013, the large enterprises (employing 250 or more persons) that dominate the pharmaceutical manufacturing industry employed 78% (424,000 people) of the total workforce of the pharmaceutical industry in the EU28 and generated 89% of the total value added. EFPIA (the industry association for European pharmaceutical enterprises) has estimated there to be an even higher number of people employed in the pharmaceutical industry, 690,000 (of whom 115,000 people are estimated to be working in R&D[275]).

Table 9-3: Employment in EU manufacturing enterprises involved in nanotechnology for health

	2005	2006	2007	2008	2009	2010	2011	2012	2013
Number of people employed ('000s)									
Pharmaceuticals	549.8	563.3	567.0	557.6	535.2	542.0	542.5	548.1	543.5
Specialised Equipment	-	-	-	50.1	48.6	53.3	53.0	53.6	54.1
Instruments and Supplies	-	-	-	479.9	458.5	483.2	502.1	490.2	480.0
Total	549.8	563.3	567.0	1087.6	1042.3	1078.5	1097.6	1091.9	1077.6

For pharmaceutical manufacturing in the EU28 in 2012, the highest value added came from Germany (19%), Ireland (15%), France (11%) and United Kingdom (10%). Ireland was the most specialised Member State with pharmaceuticals manufacturing contributing c. 15% of the Irish non-financial business economy value-added in 2010. Germany employed the largest number of people with over 121,000, followed by France (76,000), Italy (61,000), the United Kingdom (50,000) and Switzerland

[275] EFPIA (2014) Pharmaceutical Industry in Figures, 2014

(42,000).

For specialised equipment in the EU28 in 2012, the highest value-added came from Italy (19%), Germany (17.6%), France (11.3%), Denmark (10.3%) and the United Kingdom (8.5%) with Denmark being the most specialised in this sector. Italy employed the largest number of people in this sector (12,000), followed by Germany (10,000) and, at some distance, the Netherlands and Denmark (5,000 each).

For instruments and supplies in the EU28 in 2012, the highest value-added came from Germany (38.4%) with Ireland and France following at substantial distance with 13.1% and 12.1% respectively. Ireland is the most specialised EU Member State in this sector with added value of 3.7% to its non-financial business economy in 2010. By far the most people are employed by firms in Germany, 182,000 (almost 38% of total EU-28 employment in this sector).

9.1.4 EU Business R&D expenditures in health manufacturing

Looking at business R&D expenditures (BERD) in the three health manufacturing sectors in 2012, the pharmaceutical manufacturing industry spent EUR 11.5 billion on R&D in 2012 (based on figures for individual Member States). EFPIA (the industry organisation for the European pharmaceutical industry) has estimated the industry's pharmaceutical R&D as twice as high, at EUR 30.6 billion in 2013. The business R&D expenditures in the other two sectors were substantially less (each about one tenth of the pharmaceutical R&D).

According to Eurostat[276], the German pharmaceutical industry had the largest EU business R&D expenditures (EUR 4 billion), followed by Belgium (EUR 1.4 billion) and Denmark (EUR 1 billion). The Swiss pharmaceutical industry spent EUR 3.5 billion on R&D in 2012. It is interesting to note that Belgian and Danish industry have large R&D expenditures, but those countries do not belong to the most specialised Member States or host the most manufacturers. Ireland, as the most specialised Member State, has substantially lower business R&D expenditures (EUR 127 million). Germany has the largest business R&D expenditures in the other two health manufacturing sectors.

9.1.5 Innovative EU health manufacturing enterprises

From the Community Innovation Survey (CIS) 2012[277], the EU28 includes 1,678 pharmaceutical firms that considered themselves to be innovative firms (80% of the pharmaceutical firms in the CIS data). Of these innovative firms, 1,428 are product and/or process innovative firms (of which 468 are only product and/or process innovative firms). The product and/or process innovative firms spent EUR 10.2 billion on in-house R&D and EUR 5.45 billion on external R&D in 2012. There is no data available for specialised equipment or instruments and supply manufacturers in health.

9.1.6 Financing – private equity invested in EU life sciences

The figure below presents the size of the private equity investments in life sciences compared with other sectors.

[276] EUROSTAT (2015) Business enterprise R&D expenditure (BERD) by economic activity (NACE Rev. 2)
[277] http://ec.europa.eu/eurostat/web/science-technology-innovation/data/database

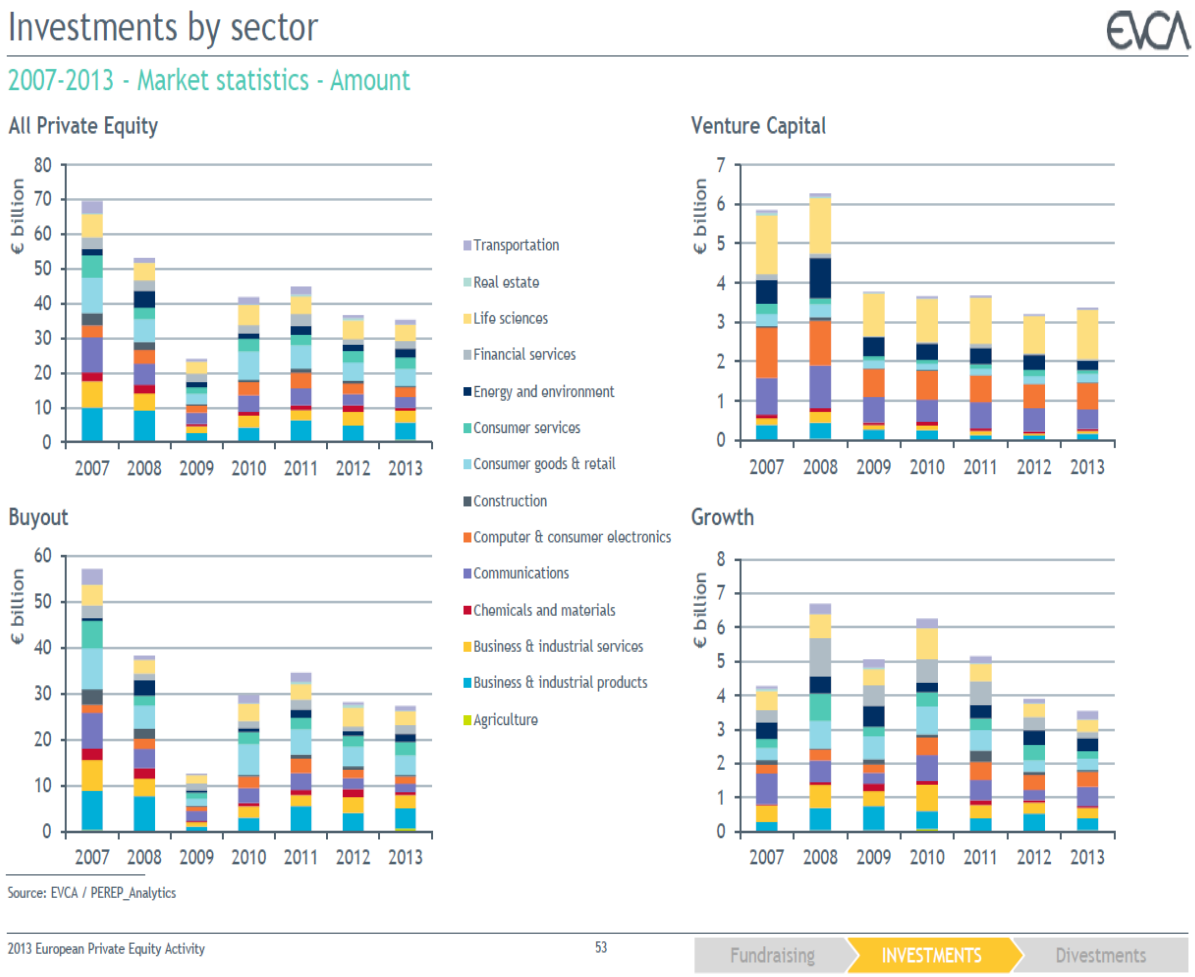


Figure 9-1: Investments by sector 2007-2013

Source: European market statistics 2007-2013, The European Private Equity & Venture Capital Association

The European Private Equity & Venture Capital Association (EVCA) (see above) has indicated that the life sciences received the highest proportion of European private equity funding in 2013 (EUR 4.68 billion, 13% of the total of EUR 35.7 billion for all sectors)[278]. About 850 life sciences companies received this private equity financing. Life sciences also received the highest proportion of venture capital funding (27% of funding, 80% of the companies).

Financing data from Ernst and Young (EY) consultants for European medical technology companies (see figure below) shows that, in 2013-2014 (12-month period), European medical technology companies attracted EUR 3.8 billion (USD 5.1 billion). Debt financing was the largest proportion (62%), while venture capital amounted to EUR 740 million (USD 1 billion, a share of 20%).

[278] EVCA (2014) 2013 European Private Equity Activity http://www.evca.eu/media/142790/2013-European-Private-Equity-Activity.pdf

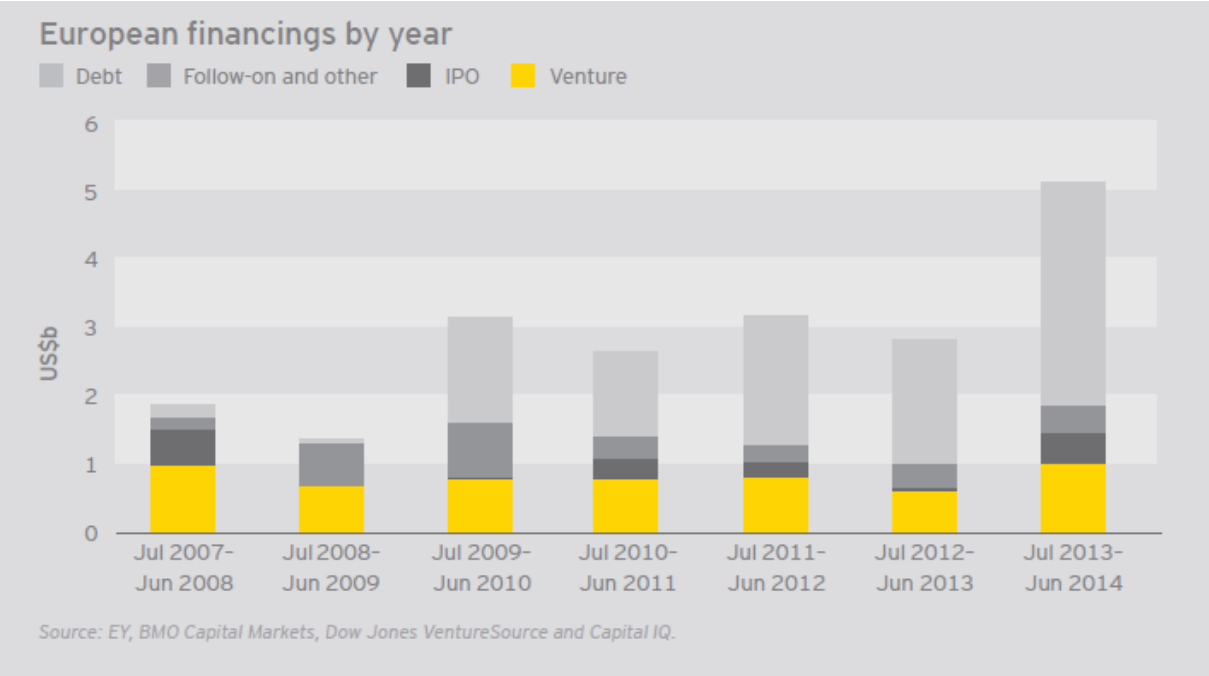


Figure 9-2: European capital markets by year

Source: EY (2014) Pulse of the Industry – Differentiating differently, Medical technology report 2014

9.2 Health nanotechnology

9.2.1 Sources of information on companies and organisations

Several sources propose numbers of enterprises active in nanotechnology for health but all use different methods and therefore arrive at different totals. Some are populated by self-selection, inviting organisations to identify themselves as working on nanotechnology and health. Others do not distinguish between companies and other types of organisations (e.g. research performing organisations). Others do not distinguish between manufacturing companies selling commercial products and organisations that are registered as companies (and may not be manufacturing).

Example of such useful sources of information include the map developed by the European Technology Platform (ETP) on Nanomedicine (NanoMed2020) which shows 747 organisations (actors) active in health nanotechnology in Europe[279]. The distribution of actors is as follows (where some occur in more than one category):

Diagnostics and imaging	210
Therapeutics and drug delivery	287
Regenerative medicine and biomaterials	84
Transversal expertise	185
Other	80

Another source is the Nanotechmap developed by Nanothinking[280]. This mapping results in a substantial lower number of actors active in nanomedicine: a total of 130 in Europe. The distribution is as follows (where some occur in more than one category):

Diagnostics & Imaging	26 + 1 in Israel
Pharmaceuticals	31 + 1 in Israel
Regenerative medicine & Biomaterials	41
Medical devices	28
Sequencing	2

[279] http://www.etp-nanomedicine.eu/public/nanomedmap/
[280] https://www.nanotechnology-collaboration.com/companies

Figure 9-3: NanoMed2020 ETP map of nanomedicine actors

Source: http://www.etp-nanomedicine.eu/public/nanomedmap/

Companies will be discussed in the section of this report on products and markets. Over 90 companies with over 100 commercial products have been identified there, the emphasis in the process of identification being mainly on the five sub-sectors, although some products coming from the broader health nanotechnology area are also included. Thus, some companies will have been omitted (but can be added in the future if appropriate). In addition, only companies with products have been included, not those with future potential products, reducing the number still further. Additional details are given in the section on *Products and Markets for Health through Nanotechnology*.

9.2.2 Estimates of employment and value added in health nanotechnology

ESTIMATES BY THE US

The US National Science Foundation[281] reported in 2008 that there were 160,000 nanotechnology workers nationally, a 25% increase over the figure in 2000. A report analysing job trends in the

[281] Roco, M. C., 2011, The long view of nanotechnology development: the National Nanotechnology Initiative at 10 years, J. Nanopart Res., 13, pp. 427-445

nanotechnology sector in the US, was published in 2007[282], the demand being based on data from advertisements, salaries and employer interviews. The supply was deduced from counts of programmes, courses and other training programmes, employment rates for graduates and the flow of talent trained in complementary fields.

The study identified

- a low demand for highly-skilled workers in the nanotechnology sector (with 296 positions identified, compared with a demand for 125,600 PhDs in similar scientific disciplines); and
- that the demand was almost entirely (97%) in academic, government or non-profit organisations.

On the supply-side, there were many training options, with over 220 institutions offering nanotechnology-related undergraduate courses. Over 5,000 doctoral graduates were emerging annually from 415 laboratories affiliated with 21 nanotechnology centres and associated with 21 universities, nearly 20% of all higher education qualifications issued in science and engineering. Indications were that the excess in supply was due to the USD 21bn investment made by the US National Nanotechnology Initiative between 2001 and 2015, further augmented by various federal programmes and venture capital investment.

The US is far from being alone in investing in nanotechnology with about 60 countries having announced its support through public funds (see the sections in this report on *Policies and Programmes*). The National Science Foundation predicted that the worldwide number of nanotechnology jobs would be approximately 2 million by 2015, employment boosted by this investment of public funds. Similar estimates have been made by the National Nanotechnology Infrastructure Network (NNIN)[283]:

Table 9-4: Worldwide nanotechnology job estimates for 2015

Country	Jobs (2015)
USA	800,000-900,000
Japan	500,000-600,000
Europe	300,000-400,000
Asia (excluding Japan)	200,000
Other regions	100,000
Total estimate	**1,900,000 – 2,200,000**

Source: National Nanotechnology Infrastructure Network (NNIN)

However, in developing these forecasts, a very broad definition of "nanotechnology" has been used, including, for example, microfabrication engineer; mems device physics engineer; principle scientist: drug delivery; business development manager-nanotech; senior researcher: bio-nanotechnology; medical device engineer; near field semiconductor engineer; research scientist: nanoscale thermal transport; and even project manager[284].

Estimate of EU employment in health nanotechnology based on the pharmaceutical industry

The number of people employed, turnover, production value, value added and business R&D expenditures for enterprises active in health nanotechnology in the EU can be roughly estimated based on the relevance of nanotechnology in the pharmaceutical industry.

Earlier in this section, three categories of health manufacturing were considered: pharmaceutical manufacturing, manufacturing of specialised equipment and manufacturing of instruments and supplies. Based on that Eurostat[285] data and NanoMed2020[286] data (as reported previously in this document), the number of people employed in therapeutics and drug delivery in health nanotechnology can be estimated. In making the estimates, it is assumed that the NanoMed category

[282] Black, G., 2007, Human Resources and Nanotechnology, Proc. Conf. Workshop on Statistics and Measurement, OECD, Paris, 14 November
[283] http://www.dummies.com/how-to/content/where-are-the-nanotechnology-career-opportunities.html
[284] http://www.masters.nano.upenn.edu/job_prospects%20.html
[285] Eurostat, Annual detailed enterprise statistics for industry (NACE Rev. 2, B-E)
[286] From the European ETP NanoMed2020

of therapeutics and drug delivery (T&DD) is equivalent to the category of pharmaceutical manufacturing. It is also assumed that most nanotechnology health firms will be rather small with 75%[287] of them having less than 250 employees.

Table 9-5: Estimate of number of employees in therapeutics and drug delivery in health nanotechnology manufacturing in the EU, 2012[288]

Pharmaceutical manufacturing (2012)	
EUROSTAT/ EFPIA	
Number of firms	4,000
Number of employees	548,100
Total value added	83.8 billion EUR
Share of employment in large firms	77.4%
Number of employees in large firms	424,300
Number of large firms	453
Average number of employees per large firm	937
Value added by large firms	72.3 billion EUR (86.3%)
Value added per large firm	159.6 million EUR
Share of employment in SMEs	22.6%
Number of employees in SMEs	123,800
Number of SMEs	3,547
Average number of employees per SME	35
Value added by SMEs	11.5 billion EUR (13.7%)
Value added per SME	3.2 million EUR
Health NT therapeutics and drug delivery firms	
NanoMed2020	
Number of health NT Firms	287
Percentage of health NT firms that are SMEs	75%
Number of health NT SMEs	215
Average number of employees per SME	35
Number of employees in health NT SMEs	7,525
Number of large health NT firms	72
Average number of employees per large firm	937
Number of employees in large health NT firms	67,464
Total number of health NT employees in therapeutics and drug delivery	74,989

Using these assumptions, the total number of employees in health nanotechnology manufacturing firms for therapeutics and drug delivery is estimated to be 74,989 (7,525 in SMEs of which there are 3,547, and 67,464 in large firms of which there are 453)[289]. It is important to note that the estimation

[287] While the proportion of small firms by number for the overall pharmaceutical industry from EUROSTAT was closer to 90%, the proportion was reduced (to 75%) to take into account the larger proportion of large firms that would be expected in a more specialised areas of therapeutics and drug delivery.

[288] Sources: EUROSTAT, EFPIA and NanoMed2020

[289] Eurostat, Annual detailed enterprise statistics for industry (NACE Rev. 2, B-E)

of employment concerns all employees, not necessarily employees that are active in nanotechnology themselves. The calculations are shown in the table above.

Similarly, EU health NT firms in nano-therapeutics and drug delivery are estimated to have achieved a value added of EUR 12.2 billion in 2012 (EUR 11.5 billion from large firms and EUR 0.7 billion from SMEs), calculated as follows:

Table 9-6: Estimated value added from EU health NT therapeutics and drug delivery[290]

Pharmaceutical manufacturing (2012)	
EUROSTAT/EFPIA	
Number of firms	4,000
Number of employees	548,100
Total value added	83.8 billion EUR
Number of large firms	453
Value added by large firms	72.3 billion EUR (86.3%)
Value added per large firm	159.6 million EUR
Number of SMEs	3,547
Value added by SMEs	11.5 billion EUR (13.7%)
Value added per SME	3.2 million EUR
Health NT therapeutics and drug delivery firms	
NanoMed2020	
Number of health NT firms	287
Percentage of health NT firms that are SMEs	75%
Number of health NT SMEs	215
Value added per SME	3.2 million EUR
Value added by health NT SMEs	688 million EUR
Number of large health NT firms	72
Value added per large firm	159.6 million EUR
Value added by large health NT firms	11.5 billion EUR
Total value added from health NT therapeutics and drug delivery	12.2 billion EUR

Based on the Eurostat[291] data and NanoMed2020[292] data (as reported previously in this document), the number of people employed in diagnostics and imaging in health nanotechnology can be estimated. In making the estimates, it is assumed that the NanoMed category of diagnostics and imaging is equivalent to the category of irradiation, electro-medical and electrotherapeutic equipment. It is also assumed that most nanotechnology health firms will be rather small with 75%[293] of them having less than 250 employees.

The estimation for the share of health NT employment in diagnostics and imaging (as it equates to irradiation, electro-medical and electrotherapeutic equipment) is as follows:

[290] Sources: EUROSTAT, EFPIA and NanoMed2020
[291] Eurostat, Annual detailed enterprise statistics for industry (NACE Rev. 2, B-E)
[292] From the European ETP NanoMed2020
[293] While the proportion of small firms by number for the overall irradiation, electro-medical and electrotherapeutic industry from EUROSTAT was closer to 90%, the proportion was reduced (to 75%) to take into account the larger proportion of large firms that would be expected in more specialised areas of diagnostics and imaging.

Table 9-7: Estimate of number of employees in diagnostics and imaging in health nanotechnology manufacturing in the EU[294]

Manufacturers of irradiation, electro-medical and electrotherapeutic equipment (2012)	
EUROSTAT/EFPIA	
Number of firms	2,039
Number of employees	53,600
Total value added	4.9 billion EUR
Share of employment of large firms	49.4%
Number of employees in large firms	26,500
Number of large firms	37[295]
Average number of employees per large firm	716
Value added by large firms	3.02 billion EUR (61.4%)
Value added per large firm	81.6 million EUR
Share of employment in SMEs	50.6%
Number of employees in SMEs	27,100
Number of SMEs	2,002
Average number of employees per SME	14
Value added by SMEs	1.9 billion EUR (38.6%)
Value added per SME	0.95 million EUR
Health NT diagnostics and imaging	
NanoMed2020	
Number of health NT firms	210
Percentage of health NT firms that are SMEs	75%
Number of health NT SMEs	158
Average number of employees per SME	14
Number of employees in health NT SMEs	2,212
Number of large health NT firms	52
Average number of employees per large firm	716
Number of employees in large health NT firms	37,232
Total number of health NT employees in diagnostics and imaging	39,444

Adding this to the total for therapeutics and drug delivery, the total employment for these two categories is 114,000 employed in the EU. Relative to the estimates made by the US National Nanotechnology Initiative (NNI), this would imply that about one third of the nanotechnology employees in Europe could be categorised as working in the health sector.

[294] Sources: EUROSTAT, EFPIA and NanoMed2020

[295] The number of large firms in the EUROSTAT data for irradiation, electro-medical and electrotherapeutic equipment is 37 while the estimate for nanotechnology firms in diagnostics and imaging is 52. Despite this difference (i.e. that the number of NT firms appears greater than the total number of firms, it should be noted that the aim here is only to use the EUROSTAT data as a benchmark for the type of firms in the NanoMed data (i.e. that the firms would have similar numbers of employees and value added) thereby enabling an extrapolation to nanotechnology firms.

A separate estimate has been made by Research in Germany[296] that around 1,000 companies (80% of them SMEs) were engaged in some form of development and marketing of nanotechnology products, methods and services in 2014 and that they employed 70,000 workers. With almost half of all European nanotechnology companies being estimated to be in Germany[297], this implies the number of nanotechnology jobs in Europe is c.150,000. If this is the case, the calculations above indicate that two thirds of the nanotechnology employees in Europe could be categorised as working in the health sector. This may, for example, indicate an over-estimation in the current calculations, an under-estimate in the calculations by Research in Germany or that workers in other sectors (e.g. transport, energy) are not seen as working in nanotechnology.

In terms of added value, health NT firms in diagnostics and imaging (D&I) are estimated to have achieved a value added of EUR 4.4 billion in 2012 (EUR 4.2 billion from large firms and EUR 0.2 billion from SMEs), calculated as follows:

Table 9-8: Estimated value added from EU health NT diagnostics and imaging[298]

Manufacturers of irradiation, electro-medical and electrotherapeutic equipment (2012)	
EUROSTAT/EFPIA	
Number of firms	2,039
Number of employees	53,600
Total value added	4.9 billion EUR
Number of large firms	37
Value added by large firms	3.0 billion EUR (61.6%)
Value added per large firm	81.6 million EUR per firm
Number of SMEs	2,002
Value added by SMEs	1.9 billion EUR (38.6%)
Value added per SME	1.5 million EUR
Health NT diagnostics and imaging	
NanoMed2020	
Number of health NT firms	210
Percentage of health NT firms that are SMEs	75%
Number of health NT SMEs	158
Value added per SME	1.5 million EUR
Value added by health NT SMEs	237 million EUR
Number of large health NT firms	37
Value added per large firm	81.6 million EUR
Value added by large health NT firms	4.2 billion EUR
Total value added from health NT diagnostics and Imaging	4.4 billion EUR

Adding this to the total for therapeutics and drug delivery, health NT firms are estimated to have achieved a value added of EUR 16.6 billion, of which EUR 15.7 billion is from large firms and EUR 0.9 billion from SMEs.

The next section reports on products, markets and companies for health nanotechnology.

[296] http://www.research-in-germany.org/en/
[297] http://www.gtai.de/GTAI/Navigation/EN/Invest/Industries/Chemicals-materials/nanotechnology.html
[298] Sources: EUROSTAT, EFPIA and NanoMed2020

10 PRODUCTS AND MARKETS FOR HEALTH THROUGH NANOTECHNOLOGY

10.1 Introduction

For the health sector, nanotechnology has the potential, for example, to:

- Increase absorption and targeting of medication;
- Reduce side effects by increasing and improving the delivery mechanisms;
- Offer new possibilities in implantation;
- Enable the combination of diagnosis and treatment in one single system; and
- Result in radical new diagnostics and therapeutics that cannot be predicted.

Current and potential future commercial applications of nanotechnology in the field of medicine and health include: implants and prosthetics, diagnostics using MEMs and sensors, drug delivery using nanoparticles, lab-on-chip, and advanced drug delivery systems. Nanotechnology can be regarded as a technology platform leading to diagnostics, pharmaceuticals and medical devices. It has the potential to help in addressing previously untreatable ailments and in detecting and treating major illnesses at earlier stages and more effectively. However, it is in the nature of health research and development that the costs of product development and delivery to the patient (including clinical trials) are high and it is necessary to have a robust demand for products to drive the growth of the market.

As a technology platform for health, achieving the promise of nanotechnology lies in boosting all kinds of research and economic initiatives in medical research and development (R&D). R&D is intensive within the areas of pharmaceuticals and medical devices, with high costs related to product development.

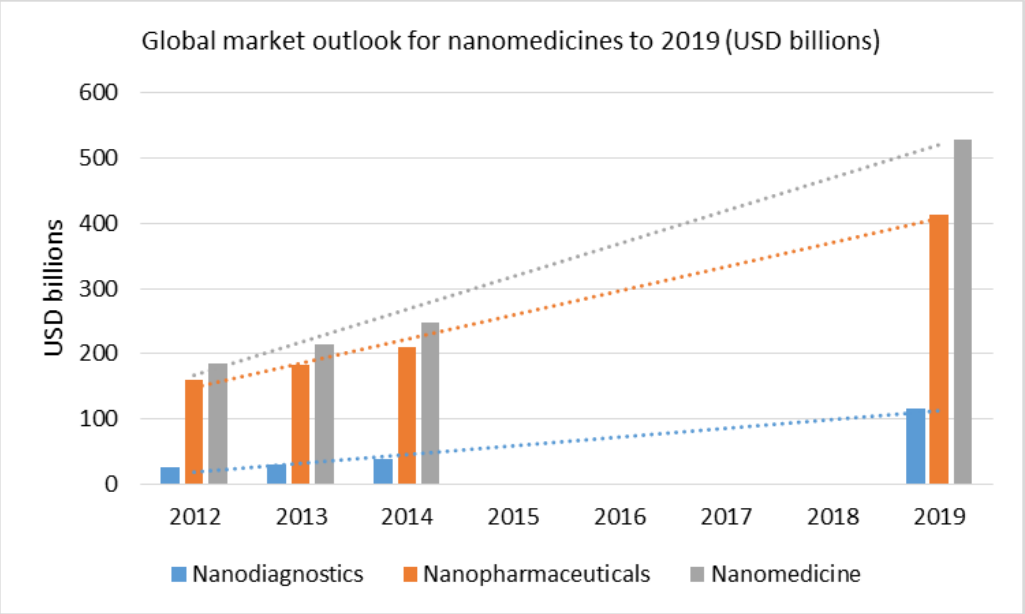
Many companies identify themselves as being active in health nanotechnology. Where their product is generic with many applications in a wide range of sectors, one of which is health, their product will often not appear as health-specific. Here, efforts have been made to identify only products that are health-specific, thereby increasing the relevance of products, but reducing their number.

The section below looks at global markets and forecasts for health products using nanotechnology.

10.2 Global markets and forecasts for health products using nanotechnology

The global market for nanomedicine products is expected to grow with a CAGR (compound annual growth rate) of 16.3% to reach a total volume of USD 528 billion in 2019 (see figure below, the dotted lines being trend lines)[299].

The nanomedicine market can be divided into two types of products, pharmaceuticals and diagnostics. In 2013, the market for nano-diagnostics was just USD 25.3 billion (11% of the total for nanomedicines) but by 2019 it is expected to be almost USD 116 billion, a growth rate (CAGR) of 24.4% (22% of the total for nanomedicines). Global sales in nano-pharmaceuticals are forecast to grow at a rate of 14.3% year on year, to rise from USD 209 billion in 2014 to USD 412 billion in 2019, a slower growth rate than for diagnostics but from a higher baseline.



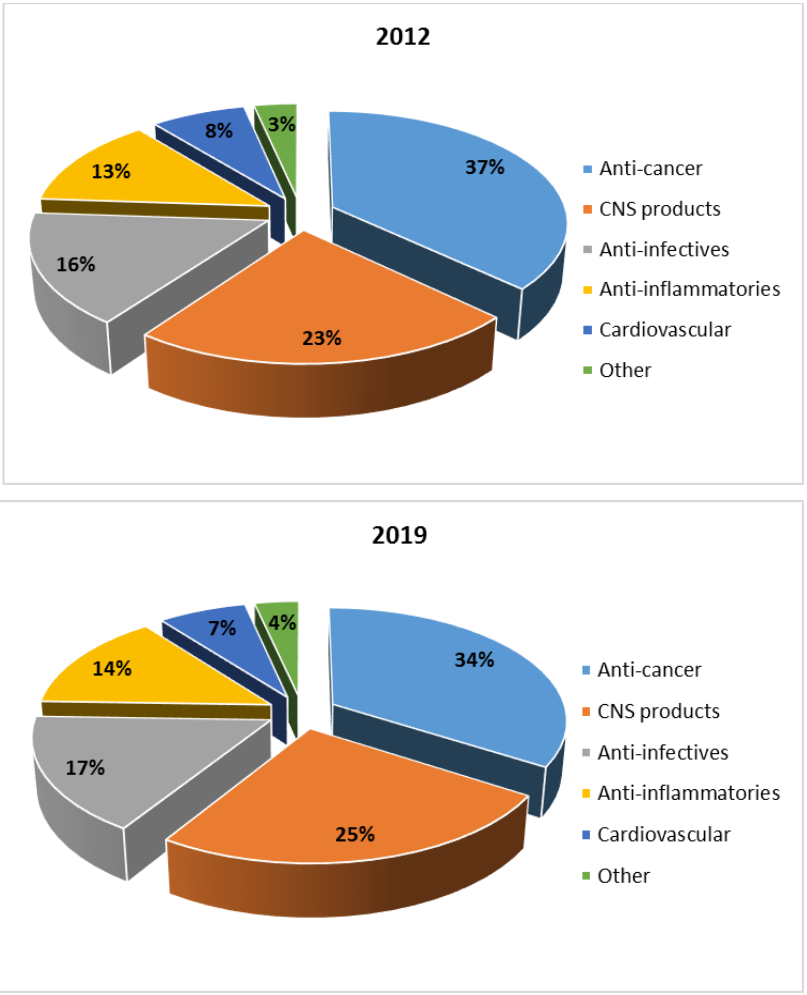
Source: BCC Research 2015

Figure 10-1: Global market outlook for nanomedicines to 2019

The relative proportions of the global market across the sub-sectors considered here (i.e. cancer, cardiovascular disease, infectious diseases and neurodegenerative diseases, data for diabetes being unavailable) are expected to change only gradually from 2012 to 2019 (see figure below). The largest share of sales is related to cancer treatment followed by central nervous system (CNS) products (largely including pharmaceuticals targeting neurodegenerative diseases) and products to prevent and counter infection ('anti-infectives').

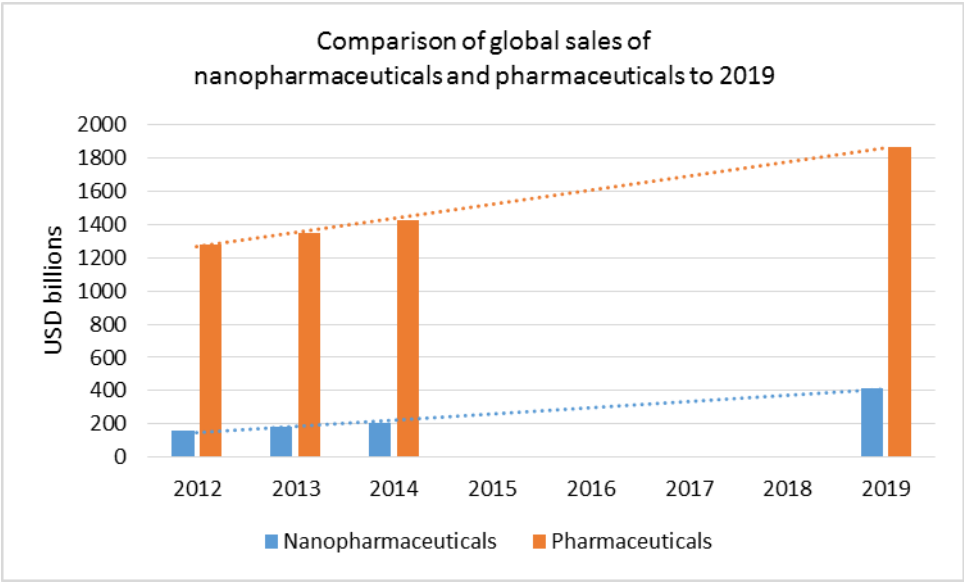
The global market for nano-pharmaceuticals is growing at a faster pace that the overall market for pharmaceuticals (see figure below). While nano-pharmaceuticals are expected to grow with a CAGR of 14.5% while the estimated figure for the overall market is 5.5%[300].

[299] BCC Research (2014), Nanotechnology in Medical Applications: The Global Market
[300] Ibid



Source: BCC Research 2015

Figure 10-2: Shares of sub-sectors in global sales of nano-pharmaceuticals, 2012 vs 2019



Source: BCC Research 2015

Figure 10-3: Global sales for nano-pharmaceuticals and pharmaceuticals forecast to 2019

The figure above illustrates that the relative shares of nano-pharmaceuticals is expected to grow from 12.5% in 2012 to 22.1% in 2019 relative to total pharmaceutical global sales.

Table 10-1: Nanotechnology and health: market estimates 2014 and 2019[301], multiple sources

	2014	2019	USD CAGR[302]	Source
	EUR (billion)	EUR (billion)	%	
Global				
Total Nanomedicine	186	498	16	BCC
Total Healthcare	73	184	12	GVR[303]
Total Nano-Diagnostics	29	109	24	BCC
Total Nano-Pharmaceuticals	157	388	14	BCC
	2014	**2019**	**USD CAGR**	**Source**
Sub-Sectors	**EUR (billion)**	**EUR (billion)**	**%**	
Cancer	24.1	--	--	F&S
Clinical Oncology		64.4	12	GVR[304]
Cardiovascular	5.3	--	--	F&S
Diabetes	5.0	--	--	F&S
Infectious Diseases	12.8	--	--	F&S
Neurodegenerative Diseases	8.3	--	--	F&S
	2014	**2019**	**USD CAGR**	**Source**
Applications	**EUR (million)**	**EUR (million)**	**%**	
Drug Delivery	117	201	7	BCC
QD for Biological Reagents	18.6	410	77	BCC
Biomarkers and Detection	70	506	42	BCC
MRI Contrast Agents (iron)	9.4	14.2	5	BCC
Surface Disinfectants	--	0.9	--	BCC
Antimicrobial Coatings	56	--	--	VDI[305]
Antibacterial lacquers	113	--	--	VDI[306]
Nano Silver for Antimicrobials	29	--	--	VDI[307]
Proteomics	--	108		BCC
Hydroxyapatite (bones/teeth)	264	1008	26	BCC
Dendrimer Transfection Reagents	0.7	6.6	51	BCC

The table above highlights available market estimates and forecasts for health nanotechnology products. There are high levels of market share and predicted growth in areas such as cancer/clinical oncology (EUR 64 billion in 2019) and synthetic bone and tooth materials (hydroxyapatite, EUR 1 billion in 2019). Other technologies are currently only emerging but are expected to show a very high growth rate to 2019: dendrimers, proteomics, bio-markers and quantum dots for bio-reagents.

[301] Original figures in USD. Conversion for 2014 at rate of 1.33 EUR per USD and for 2019 at current conversion rates 0.94 EUR per USD.
[302] Compound annual growth rate CAGR based on USD figures (i.e. does not incorporate change in EUR/USD currency exchange rate)
[303] Estimate for 2012 (not 2014), Forecast for 2020 (not 2019), CAGR for 2012-2020. Global View Research Inc.: http://www.grandviewresearch.com/industry-analysis/healthcare-nanotechology
[304] Forecast for 2020 (not 2019). Global View Research Inc.: http://www.grandviewresearch.com/industry-analysis/healthcare-nanotechology
[305] Estimate for 2013
[306] Estimate for 2013
[307] Estimate for 2013

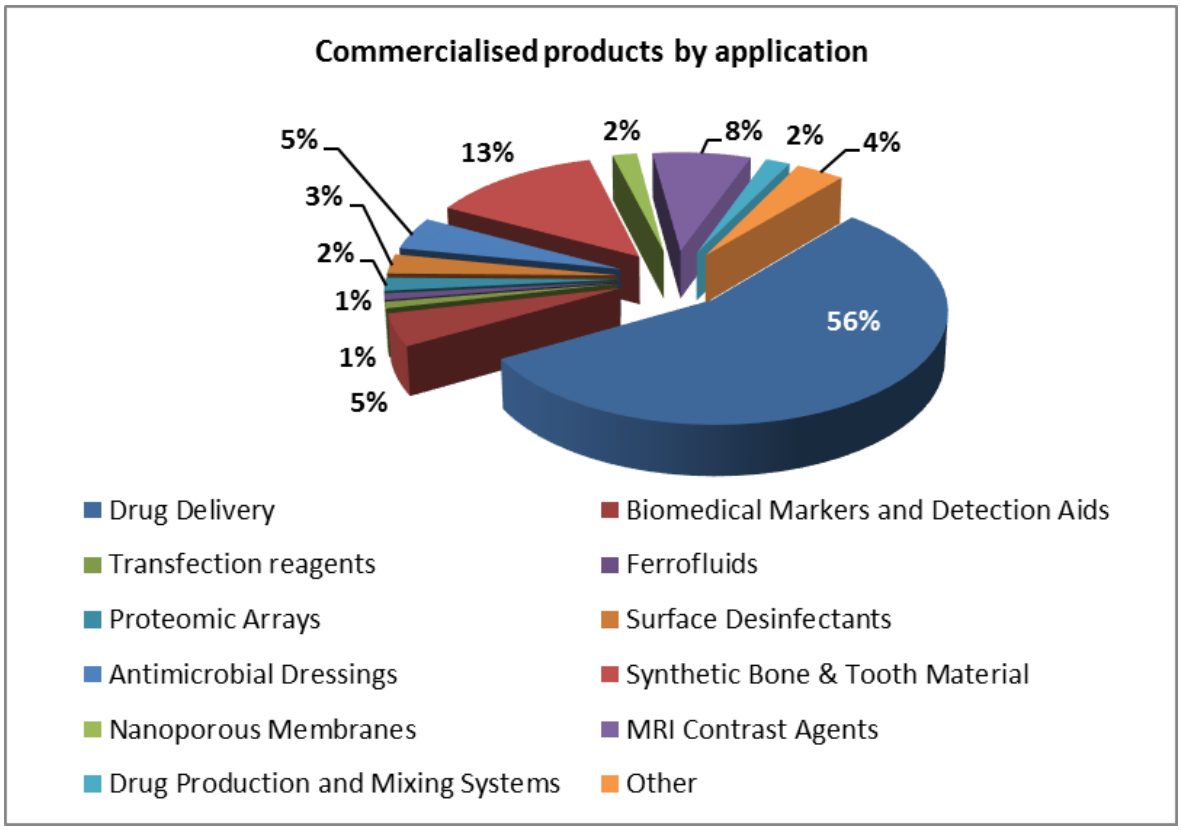
These are considered in greater detail in the remainder of the chapter.

The section that follows explores these markets in greater detail, beginning in each case with the technology and products (including company examples) and concluding with market estimates and forecasts. Company snapshots and company case studies are included. In addition, where appropriate, information is presented on likely future products and markets. First there is an overview of the products.

10.3 Commercialised products - overview

Etheridge et al. (2013) identified 147 nanomedicine applications and products, confirmed and likely, of which 100 had reached the stage of approval for commercialisation[308].

To date, 106 commercially available products have been identified as being on the market. The largest share of products (56%) is made up of nano-pharmaceuticals (i.e. drug delivery). Synthetic bone and tooth materials account for the second largest share (13%) (see figure below).

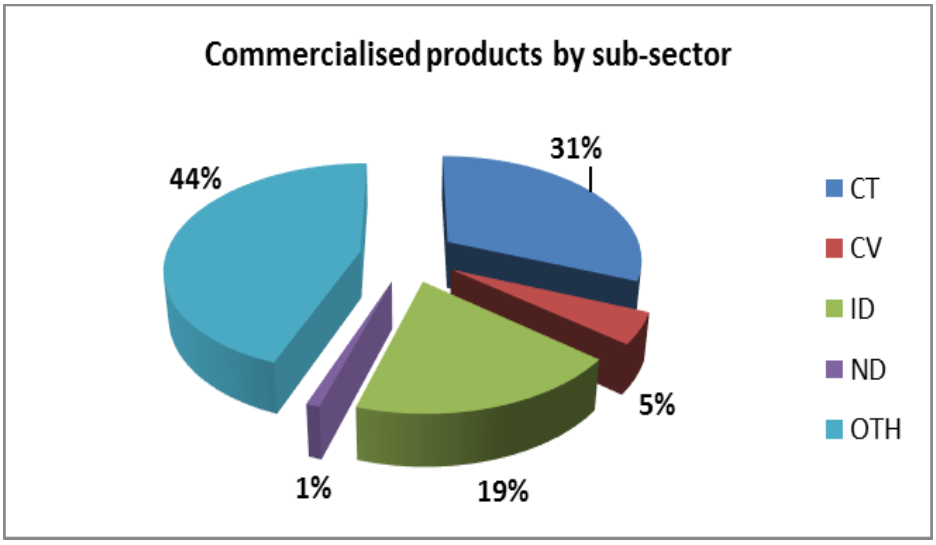


Source: JIIP, 2015

Figure 10-4: Number of identified products by commercial application market

The products are unevenly distributed among the sub-sectors, as seen in the figure below. Cancer treatment (CT) is the second largest sub-sector in terms of products (31%), infectious diseases (ID) account for 19% of the products on sale. No commercially available product could be identified in the sub-sector diabetes.

[308] Etheridge ML, et al (2014), The big picture on nanomedicine: the state of investigational and approved nanomedicine products. Nanomedicine: Nanotechnology, Biology, and Medicine 9 (2013): 5



Source: JIIP, 2015

Figure 10-5: Number of identified products by sub-sector

10.4 Products for health through nanotechnology, by commercial application market

For the discussion of trends related to products and commercial application markets, the table below provides an overview of intersections between our defined sub-sectors and commercial application markets based on existing data[309]. Black dots indicate where data is available and products exist.

In total, eleven commercial application markets could be identified, distributed across the sub-sectors of cancer treatment (CT), cardiovascular diseases (CV), infectious diseases (ID), and other. No data is available on markets for pharmaceutical and medical devices related to diabetes (DB) or neurodegenerative diseases (NE).

Each one of the eleven commercial application markets of nanotechnology for health identified in the table below is considered in more detail below by product type:

- Drug delivery vehicles (nanoparticles);
- Biomedical markers and detection aids (nanoparticles);
- Ferrofluids (nanoparticles);
- MRI contrast agents (nanoparticles);
- Surface disinfectants (nanoparticles);
- Proteomics applications (nanoparticles);
- Synthetic bone and tooth enamel (nanoparticles);
- Transfection reagents (nanoparticles);
- Nano-porous membranes (thin films and coatings);
- Antimicrobials (thin films and coatings); and
- Drug production and mixing systems (devices).

In each case, there is a description of the technology (e.g. drug delivery); its application to each of the sub-sectors by disease type (e.g. drug delivery for cancer treatment, drug delivery for cardiovascular disease, etc.); market data and forecasts (e.g. for drug delivery in nanotechnology and health); and a case study (and/or snapshot) of a company marketing one or more products.

[309] BCC Research (2014), Nanotechnology, a realistic market assessment.

Table 10-2: Commercial applications in nanotechnology health sub-sectors

		CT	CV	DB	ID	NE	Other
Nanoparticles	Drug delivery vehicles	●	●		●		●
	Biomedical markers and detection aids	●	●		●		
	Ferrofluids	●					●
	MRI contrast agents	●					
	Surface disinfectants				●		
	Proteomics applications						●
	Synthetic bone and tooth enamel						●
	Transfection Reagents						●
Thin Film & Coating	Nanoporous membranes						●
	Antimicrobials				●		
Nano-devices	Drug production and mixing systems						●

Source: JIIP, 2015

10.4.1 Drug delivery vehicles

Nanomaterials fall into a size range similar to proteins and other macromolecular structures found inside living cells. As such, nanomaterials are able to take advantage of existing cellular machinery to facilitate the delivery of drugs. Nanoparticles (NPs) containing encapsulated, dispersed, absorbed or conjugated drugs have unique characteristics that can lead to enhanced performance in a variety of dosage forms. When formulated correctly, drug particles are resistant to settling and can have higher saturation solubility, rapid dissolution and enhanced adhesion to biological surfaces, thereby providing rapid onset of therapeutic action and improved bioavailability[310].

Many of the current nano drug delivery systems are derived from conventional drug delivery systems existing in the nanometre range, such as liposomes, polymeric micelles, nanoparticles, dendrimers and nanocrystals. Liposomes and polymer micelles were first prepared in 1960's, and nanoparticles and dendrimers in 1970's. Colloidal gold particles in nanometre sizes were first prepared by Michael Faraday more than 150 years ago, but were never referred to or associated with nanoparticles or nanotechnology until recently[311].

Drug delivery by disease type

Nanotechnology is used in drug delivery systems for cancer treatment, cardiovascular disease, infectious diseases and other diseases. They also have the potential to be used in neurodegenerative disease and diabetes but no commercial products were identified.

A DRUG DELIVERY FOR CANCER TREATMENT

One of the major challenges in drug delivery is to get the drug at the place it is needed in the body thereby avoiding potential side effects to non-diseased organs. This is especially challenging in cancer treatment where the tumour may be localised as distinct metastases in various organs. The non-restricted (cyto)toxicity of chemotherapeutics thus limits the full use of their therapeutic potential. Local drug delivery or drug targeting results in increased local drug concentrations and provides

[310] Bamrungsap S, et al. (2012), Nanotechnology in Therapeutics. Nanomedicine 2012;7(8): 1253
[311] Park, K (2007), Nanotechnology: What it can do for drug delivery. J Control Release, 2007 July 16; 120(1-2): 1

strategies for more specific therapy. Nanoparticles have specific particles as tools to enable these strategies. These include benefits such as their small size which allows penetration of cell membranes, binding and stabilisation of proteins, and lysosomal escape after endocytosis[312] (i.e. the nanoparticles are not broken down in the degradation factory – the lysosome - of the cell).

ABRAXANE® by Celgene[313] (Summit, NJ, USA) is currently the only albumin-based nanotechnology therapy approved for the treatment of metastatic breast cancer, non-small cell lung cancer and pancreatic cancer in the United States, Europe and other markets around the world. It contains albumin-bound paclitaxel nanoparticles (paclitaxel is better known as the cytostatic Taxol, the active part of the taxus tree that inhibits cell division) and is manufactured using patented nab® technology. ABRAXANE is formulated with albumin, a human protein, and does not contain solvents. ABRAXANE was first approved in January 2005 by the U.S. Food and Drug Administration (FDA) for the treatment of breast cancer patients who experienced failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. In Europe, ABRAXANE was approved in January 2008 as monotherapy for the treatment of metastatic breast cancer in adult patients who have failed first-line treatment for metastatic disease and for whom standard, anthracycline-containing therapy is not indicated.

HER2-positive breast cancer is the second most common cancer in the world and the most common cancer in women worldwide. Kadcyla is a combination of an antibody and a drug (a so called antibody-drug conjugate) produced by F. Hoffmann-La Roche AG[314] (Basel, Switzerland). The conjugate consists of the antibody trastuzumab covalently linked to the cytostatic drug (a microtubule inhibitor), DM1 (mertansine). Kadcyla (ado-trastuzumab) is Roche's third HER2-targeted mAb, approved by the FDA in February 2013, by the Japanese MHLW in September 2013, and by the EMA in November 2013, for the second-line treatment of metastatic HER2-positive breast cancer.

B DRUG DELIVERY FOR CARDIOVASCULAR DISEASE

Fenofibrate, marketed under various trade names, is a popular anti-cholesterol medication (used to reduce the amount of lipids (fats) in the blood). It is known for its poor uptake when taken orally, requiring it to be dosed with food. Several dosage forms of fenofibrate are currently available[315]. Various manufacturers of fenofibrate have aimed to improve formulations by decreasing particle size in efforts to increase solubility and (bio)availability[316].

One such fenofibrate is that of TRICOR tablets for oral administration, produced by Abbott Laboratories[317] (North Chicago, IL, USA). Each tablet contains 54 mg or 160 mg of fenofibrate in NanoCrystal™ formulation. NanoCrystal™ technology is a drug optimisation technology applicable to poorly water-soluble compounds developed by Elan. It is covered by numerous US and international patents and patent applications and is part of a suite of technologies that the company EDT offers to third-party clients. NanoCrystal technology is used to reduce crystalline drug to particles under 400 nanometres. By reducing particle size, the exposed surface area of the drug is increased and is then stabilised to maintain particle size. The drug in nano-form can be incorporated into common dosage forms, including tablets, capsules, inhalation devices, and sterile forms for injection, with the potential for substantial improvements to clinical performance.

Triglide® made by Skyepharma[318] (London, UK) is a competing product based on a nanocrystal formulation of fenofibrate, an oral treatment for elevated blood lipid disorders, marketed in the US by Shionogi Pharma[319] (Florham Park, NJ, USA). It was formulated using Skyepharma's proprietary Insoluble Drug Delivery (IDD®) technology to allow the product to be taken independently of food ingestion[320].

C DRUG DELIVERY FOR INFECTIOUS DISEASES

[312] De Jong WH, Borm PJA (2008), Drug delivery and nanoparticles: Applications and hazards. International Journal of Nanomedicine 2008 Jun; 3(2): 134
[313] www.celgene.com
[314] www.roche.com
[315] Weissig V, et al. (2014), Nano-pharmaceuticals (part 1): products on the market. International Journal of Nanomedicine 2014 (9): 4364
[316] Ling H, et al. (2013), A review of currently available fenofibrate and fenofibric acid formulations. Cardiol Res. 2013; 4(2): 47.
[317] www.abbott.com
[318] www.skyepharma.com/
[319] www.shionogi.com/
[320] http://www.skyepharma.com/Technologies/Oral_drug_delivery_technologies/Bioavailability_enhancers

AmBisome (amphotericin B liposomal) by Gilead Sciences[321] (Foster City, CA, USA) is an antifungal medication that fights infections caused by fungus. AmBisome for Injection is a product for intravenous infusion. AmBisome is used to treat serious, life-threatening diseases caused by fungi and parasites, including leishmaniasis and a certain form of meningitis in people infected with HIV (human immunodeficiency virus). AmBisome is a single bi-layer liposomal drug delivery system. Liposomes are closed, spherical vesicles consisting of lipids and cholesterol arranged into concentric bilayer membranes that can be used as a vehicle for administration of e.g. pharmaceutical drugs. AmBisome consists of these bi-layer liposomes with amphotericin B intercalated within the membrane. Due to the nature and quantity of substances used, the drug is an integral part of the overall structure of the AmBisome liposomes. AmBisome contains true liposomes that are less than 100 nm in diameter[322].

Peg-Intron (peginterferon alfa-2b) Powder for Injection by Schering-Plough (now MSD Sharp & Dohme[323] in Kenilworth, NJ, USA) has been approved by the FDA in 2001 as a once-weekly monotherapy for the treatment of chronic hepatitis C. Hepatitis C is a liver disease caused by the hepatitis C virus, which is spread by contact with the blood of an infected person. It is indicated for patients with compensated liver disease who were not previously treated with alpha interferon. Peg-Intron is the first pegylated interferon to be approved in the United States, and therefore offers a new treatment option for hepatitis patients. PEG-interferon alpha is a pegylated interferon composed of 165 amino acids. The PEG (polyethylene glycol) protects the molecule from proteolytic breakdown and increases the biological half-life of the interferon protein. It has also been approved as treatment for melanoma with nodal involvement after surgical resection, under the brand name Sylatron by MSD Sharp & Dohme in April 2011.

D DRUG DELIVERY FOR OTHER DISEASES

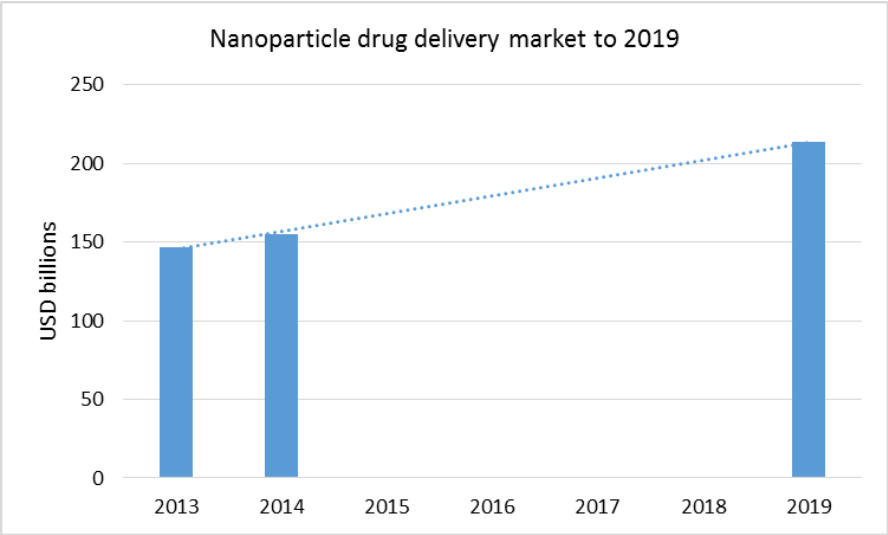
ADAGEN® (pegademase bovine) Injection by Sigma Tau Pharmaceutical Inc.[324] (Pomezia, Italy) is used to treat patients afflicted with a type of Severe Combined Immunodeficiency Disease (also known as SCID or the "Bubble Boy Disease"), which is caused by the chronic deficiency of the adenosine deaminase (ADA) enzyme. Children with SCID, a rare disease, are born without fully functioning immune systems, which leaves them susceptible to a wide range of infectious diseases. ADAGEN is indicated for enzyme replacement therapy for ADA deficiency in patients with severe combined immunodeficiency disease who are not suitable candidates for or who have failed bone marrow transplantation. ADAGEN is a PEGylated version of the ADA enzyme and represents the first successful application of enzyme replacement therapy for an inherited disease. It is a valuable life-saving treatment option that provides predictable restoration of ADA activity to ADA SCID patients[325].

Macugen™ (Pegaptanib sodium injection) is an anti-angiogenic medicine for the treatment of neovascular (wet) age-related macular degeneration (AMD)[326]. It was discovered by NeXstar Pharmaceuticals and licensed in 2000 to EyeTech Pharmaceuticals, now OSI Pharmaceuticals[327] (Long Island, NJ, USA), for late stage development and marketing in the United States. Outside the US pegaptanib is marketed by Pfizer Inc.[328] (New York City, NY, USA). Approval was granted by the U.S. Food and Drug Administration (FDA) in December 2004[329]. Pegaptanib is a pegylated anti-vascular endothelial growth factor (VEGF) aptamer, a single strand of nucleic acid that binds with specificity to a particular target. Pegaptanib specifically binds to the 165 isoform of VEGF, a protein that plays a critical role in angiogenesis (the formation of new blood vessels) and increased permeability (leakage from blood vessels), two of the primary pathological processes responsible for the vision loss associated with neovascular AMD. Pegaptanib works as an antagonist to VEGF, which when injected into the eye blocks the actions of VEGF. This then reduces the growth of the blood vessels located within the eye and works to control the leakage and swelling[330].

MARKET DATA AND FORECASTS FOR DRUG DELIVERY IN NANOTECHNOLOGY AND HEALTH

[321] www.gilead.com/
[322] Gilead Sciences, Inc., 2012, AmBiSome product description
[323] www.merck.com
[324] www.sigmatau.com/
[325] ADAGEN® (pegademase bovine) Injection, Product Sheet
[326] European Medicines Agency: EMA/671614/2010
[327] www.osip.com
[328] www.pfizer.com
[329] "Highlights of Prescribing Information (Macugen)" Food and Drug Administration: 3–12. July 2007
[330] Ibid

It is estimated[331] that the total market for nanoparticle drug delivery vehicles was about USD 147 million in 2013 and more than USD 155 million in 2014, increasing to nearly USD 214 million by 2019, a CAGR of 6.6% over five years.



Source: BCC Research, 2014

Figure 10-6: Nanoparticle drug delivery market to 2019, USD billions

Case study: drug delivery in nanotechnology and health: Flamel Technologies

Flamel Technologies SA[332], based out of France, is a specialty pharmaceutical company focusing on drug delivery and formulation. The company was incorporated in 1990 and became a public company in 1996. The company has survived but not truly thrived over the 19 years since becoming a public company. However, the company is being turned around, with many positive indications and characteristics that their story will lead to future commercial success.

Until recently, the strategy of the company was to carry out formulation development for major pharmaceutical companies, receiving a royalty in exchange for any products that advanced to NDA (new drug application) approval. Their most successful product was a controlled-release version of GlaxoSmithKline's (GSK) beta-blocker, Coreg CR (for the treatment of heart failure). Since they were under working relationships with GSK and others, Flamel did not apply for European Framework funding under the FP6 or FP7 programmes. They currently have no funding from the European Commission nor any public funds from the French Government.

In March 2012, Flamel made the game-changing acquisition of Eclat Pharma, obtaining a pipeline of four "unapproved but marketed" drugs. It has undergone a significant shift since this acquisition and is now a more vertically integrated specialty pharmaceutical company. As a result, it expects to generate substantial product revenues in 2015-2016.

With its primary focus on drug delivery platforms, Flamel has spent USD 17.3 (EUR 13.0) million on R&D with annual revenues of USD 180 (EUR 135) million in 2014. Nanotechnology related R&D activities accounted for USD 3.4 (EUR 2.6) million with 75 R&D staff assigned to various projects under this area across its 3 sites in Vénissieux (France), Dublin (Ireland) and Chesterfield (USA). With product revenues expected to come in soon, the company plans to double its focus on nano-related activities in the next three years.

Flamel has four approaches to improving drug delivery, through which they can cover a wide range of dosage forms as shown in the schematic below. Medusa is a new technology for extended release of drugs via subcutaneous delivery, while Micropump, LiquiTime, and

[331] BCC Research (2014), Nanotechnology, a realistic market assessment. p. 120
[332] www.flamel.com/

TriggerLock all use the same microparticle extended-release technology for oral formulations.

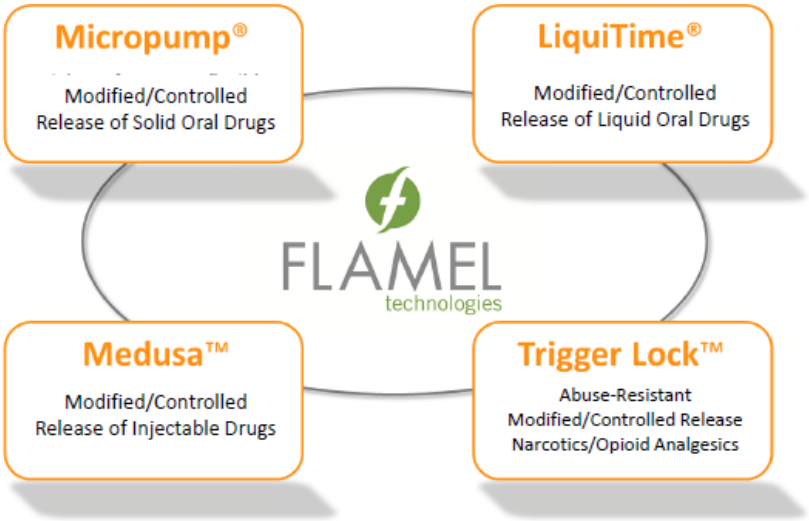


Figure: Flamel's approach to Drug Delivery

Flamel has developed Medusa™ Exenatide for treatment of Type II Diabetes, covered under Patent No. US 20110150837 A1 until June 2031. This drug delivery platform consists of proprietary nanogels for the formulation and/or the extended release of a broad range of biologics (including proteins, antibodies, peptides and vaccines) and of small molecules. It is amphiphilic[333] and spontaneously forms stable nanoparticles in water. Flamel's 2014 annual revenue was around USD 180 (EUR 135) million and 22% of this (USD 39.6 million, EUR 29.7 million) is estimated to be linked to Medusa.

Since the acquisition of Éclat, Flamel has been implementing a business model combining the commercialisation of niche branded pharmaceuticals (Bloxiverz® and Vazculep®) and generic pharmaceuticals in the US and other countries as appropriate. Most of these opportunities are self-funded. By adopting this new strategy, Flamel is making itself less dependent on the often-changing strategies of larger partners.

Flamel interacts with a number of organisations and benefits from its involvement with clusters such as the Lyonbiopôle (a competitiveness cluster supported by the French State). As part of this cluster, Flamel is able to tap into expertise in areas from diagnostics and prevention to treatment, resulting in the continuing development of innovative delivery systems. Within this cluster, Flamel also interacts with Sanofi Pasteur, Beckton Dickinson and bioMérieux (although details of the working relationship with these large firms are under non-disclosure agreements). Flamel is still exploring development, supply and licensing opportunities for either its drug delivery platforms or its proprietary products with third parties but, since it has changed its strategy, it is no longer completely dependent on these partnerships in creating revenue and profit opportunities.

Flamel works actively with regulatory authorities and other agencies, providing opinions and feedback in its areas of operation, for example, to the European Commission on Variations Regulations.

10.4.2 Biomedical markers and detection aids

Nanotechnology-enabled biomedical markers and detection aids make use of modified or engineered nanoparticles to assist in the identification or visualisation of target analytes[334] or anatomical/biological structures. Nanoparticles that are typically used for such applications are gold, dendrimers, quantum dots and iron oxides.

Biomedical markers and detection aids use nanotechnology against cancer, cardiovascular disease

[333] Amphiphilic: possessing both hydrophilic (water-loving, polar) and lipophilic (fat-loving) properties
[334] Compounds that are to be identified, measures and/or analysed.

and infectious diseases.

A BIOMEDICAL MARKERS AND DETECTION AIDS AGAINST CANCER

Circulating tumour cells (CTCs) are cells that have shed into the vasculature from a primary tumour and circulate in the bloodstream. CTCs thus constitute seeds for subsequent growth of additional tumours (metastasis) in vital distant organs, triggering a mechanism that is responsible for the vast majority of cancer-related deaths[335]. Detection aid for CTCs is based on a method using iron nano-particles coated with a polymer layer carrying biotin analogues and conjugated with antibodies anti EpCAM for capturing CTCs, and on the use of an analyser to take images of isolated cells upon their staining with specific fluorescent antibody conjugates[336].

Veridex LLC (now Janssen Diagnostics[337] in Raritan, NJ, USA) introduced its CellSearch Epithelial cell kit in 2004 which is based on magnetic iron oxide nano particles. The CellSearch CTC assay uses peripheral whole blood for the detection, enrichment and quantification of CTC of epithelial origin. CTC measurement helps oncologists to determine the prognosis, in predicting cancer progression and to monitor therapy in the management of patients with metastatic breast, prostate and colorectal cancers. It contains an anti-EpCAM ferrofluid capture reagent and immunofluorescent reagents. The anti-EpCAM ferrofluid reagent consists of anti EpCAM magnetic beads which target the EpCAM antigen expressed by some types of epithelial tumours.

CellTracks® introduced by Immunicon Corp. in 2003 has been working on a similar basis but in 2008 Immunican has been taken over by Veridex (Veridex and Immunicon have partnered since 2000 to develop and commercialise novel cancer diagnostic platforms and products).

B BIOMEDICAL MARKERS AND DETECTION AIDS FOR CARDIOVASCULAR DISEASES

Dendrimers are highly branched, star-shaped macromolecules with dimensions at the nanoscale. Dendrimers are defined by three components: a central core, an interior dendritic structure (the branches), and an exterior surface with functional surface groups. The varied combination of these components yields products of different shapes and sizes with shielded interior cores that are ideal candidates for applications in both biological and materials sciences. While the attached surface groups affect the solubility and chelation ability, the varied cores impart unique properties to the cavity size, absorption capacity, and capture-release characteristics. Applications highlighted in recent literature include drug delivery, gene transfection, catalysis, energy harvesting, photo activity, molecular weight and size determination, rheology modification, and nanoscale science and technology[338].

Dade Behring (now Siemens AG[339] in Munich, Germany), a clinical diagnostics company headquartered in Deerfield, Ill., has been using dendrimers in its diagnostic technology since 1998. The molecules are a key component in the company's Stratus CS instrument for cardiac analysis[340]. Dade-Behring uses dendrimers provided by Dow Chemical Co.[341] (Midland, Mich., USA) in its Stratus CS cardiac analyser system to bind the captured antibody to the solid phase and provide a high degree of analytical sensitivity and precision. The Stratus CS is a fluorometric enzyme immunoassay analyser based on solid-phase radial partition immunoassay technology, which performs quantitative measurements of the cardiac markers CK-MB, myoglobin and troponin-I in whole blood samples[342]. The technology uses antibodies immobilised on a specimen tester made of glass fibre paper as part of the biomarker detection system, according to Singh. And it's the dendrimers that anchor these antibodies to the glass. The fifth-generation PAMAM dendrimers that the Stratus CS employs are positively charged. Each antibody is covalently linked to the dendrimer, which is immobilised on the negatively charged glass through electrostatics[343].

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[335] Gupta GP, Massagué J (2006), Cancer metastasis: building a framework. Cell 127 (4): 679.
[336] An Introduction to CellSearch; https://www.cellsearchctc.com/
[337] www.janssen.com/
[338] Functional Polymers and Dendrimers: From Synthesis to Application. Proceedings of the American Chemical Society Division of Polymeric Materials: Science & Engineering, San Diego, CA, April 1-5, 2001; ACS, 2001
[339] www.siemens.com
[340] Halford B (2005), Dendrimer Branchout. Chemical & Engineering News, June 13, 2005 Volume 83, Number 24: 30
[341] www.dow.com/
[342] Heeschen C (2000), Evaluation of a Rapid Whole Blood ELISA for Quantification of Troponin I in Patients with Acute Chest Pain. Clinical Chemistry July 2000 vol. 46 no. 7: 992
[343] Halford B (2005), Dendrimer Branchout. Chemical & Engineering News, June 13, 2005 Volume 83, Number 24: 30

c BIOMEDICAL MARKERS AND DETECTION AIDS FOR INFECTIOUS DISEASES

Nanosphere, Inc.[344] (Northbrook, IL, USA) has developed an innovative system called Verigene®, a workstation for molecular diagnostics that uses patented technology of colloidal gold nanoparticles. The system has been introduced in 2007 to the market and is able to detect the target nucleic acid useful for a range of applications[345]. The Verigene System includes a bench-top molecular diagnostics workstation that is a universal platform for genomic and protein testing. The Verigene System provides for multiple tests to be performed on a single platform, including both genomic and protein assays, from a single sample. The Verigene System is comprised of a microfluidics processor, a touchscreen reader, certain disposable consumables used in sample preparation, target amplification and test cartridges.

MARKET DATA AND FORECASTS FOR BIOMARKERS AND DETECTION AIDS[346]

It has been estimated that the global consumption of nanoparticles used in biomedical marker and detection applications was over USD 78 million in 2013. This total includes colloidal gold, dendrimers, iron oxide and quantum dots. Each type of nanoparticle is used in different types of tests, so the market drivers and projected growth rates vary (see table below)[347].

Table 10-3: Global consumption of nanoparticles in biomedical marker and detection applications to 2019

	Global Consumption (USD million)			CAGR% 2014-2019
	2013	2014	2019	
Colloidal Gold	55.0	57.5	71.6	4.5
Quantum Dots	14.0	24.8	435.0	77.3
Iron oxide	8.4	10.1	25.1	20.0
Dendrimers	1.0	1.3	4.8	29.9
TOTAL	78.4	93.7	536.5	41.8

Source: BCC Research, 2014

Colloidal gold consumption for bio-labelling applications is forecast to grow with a CAGR of 4.5% over the near to mid-term, with sales of USD 57.5 million in 2014 and USD 71.6 million in 2019.

In 2013, quantum dots (semiconductor nanoparticles) accounted for about 0.2% (USD 14 million) of the estimated USD 7 billion global market for fluorescence-based biological reagents. The overall market being expected to more than double by 2019 (rising to USD 14.5 billion) and the quantum dot share being expected to grow to as much at 3% of that market, the forecast is for fluorescence-based biological reagents using quantum dots to be USD 435 million in 2019[348].

For clinical diagnostics as a whole, the sales of diagnostic reagents are equivalent to an estimated 37.5% of instrument sales. Applying this to superparamagnetic clinical diagnostic instrument sales gives reagent sales of USD 8.4 million in 2013. The market for iron oxide nanoparticles for bio-magnetic separation applications is projected to grow at a CAGR of 20% from 2014 through 2019.

Dendrimer sales in 2013 were USD 1 million, the forecast being for a growth rate (CAGR) of 15%. If new diagnostics applications emerge as expected, there could be a doubling of market share for reagents containing dendrimers, a CAGR of about 30%, leading to a market value of USD 48 million by 2019, or USD 4.8 million for the dendrimers themselves.

[344] www.nanosphere.us/
[345] http://www.moss-info.it/en/products/verigene-system-2/
[346] BCC Research (2014), Nanotechnology, a realistic market assessment. p. 124
[347] Ibid
[348] ibid

Case study: biomedical markers and detection aids in nanotechnology and health: BioNano Genomics[349]

BioNano Genomics was formed in 2003 as BioNanomatrix Inc., and changed its name to BioNano Genomics in 2011. Its principal technology is next-generation sequencing (NGS), a technology that has emerged over time as the de facto genetic research tool. While NGS has enabled significant discoveries, its short reads cannot effectively resolve the massive repeat segments and structural variations in genomes, leaving large holes in the genetic puzzle.

BioNano Genomics' next-generation mapping (NGM) system is called the Irys® System. It makes possible the acquisition of whole genome maps in days at a fraction of its previous cost before (down from c. USD 100,000 (c EUR 72,000) in 2009 to USD 1,000 (c. EUR 900) with Irys system. Irys detects structural variations in a patient's genetic structure - including DNA insertions, deletions and repeats.

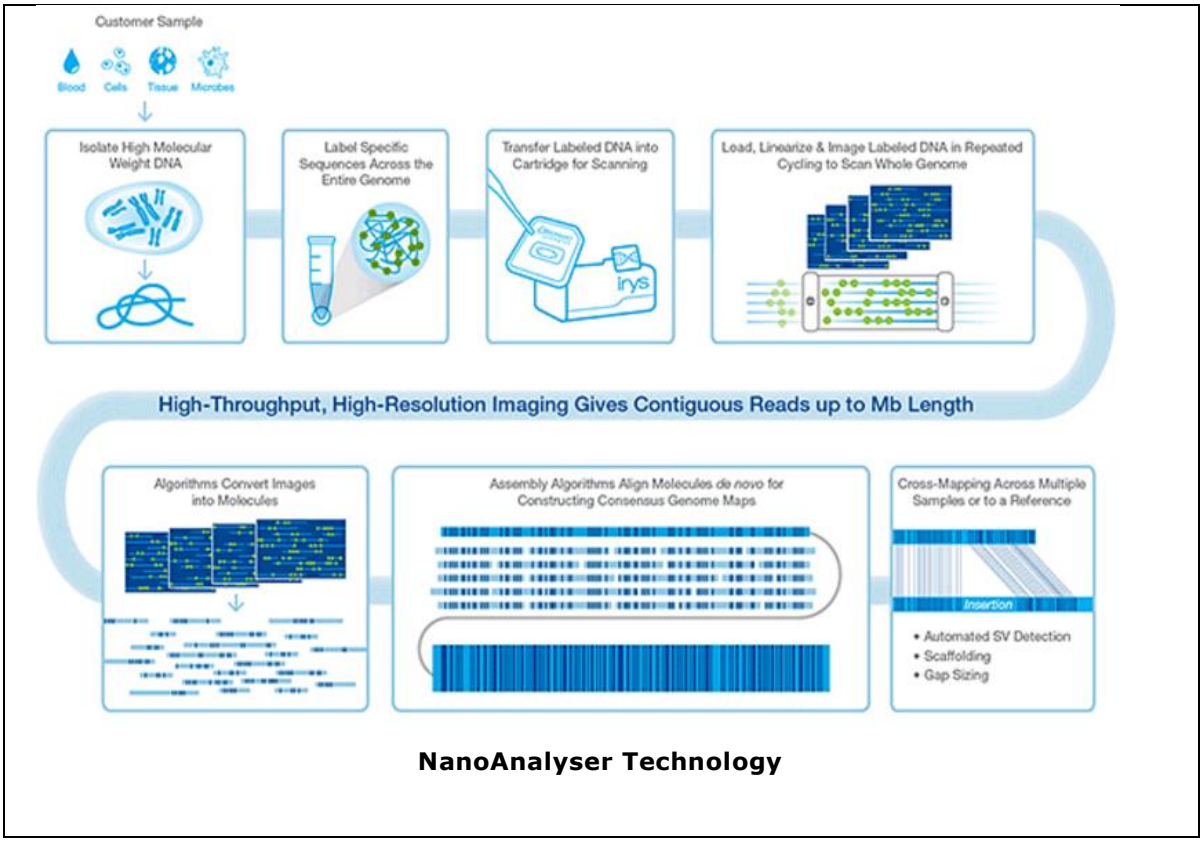
BioNano Genomics relies on a single-molecule genomic analysis technology for its NanoAnalyzer® system. The core technology is covered by U.S. patent 7,670,770 issued to Princeton University in 2010 on which BioNano Genomics has worldwide exclusive license. The purpose of the technology is to enhance whole genome imaging and analysis for a wide range of research and diagnostic applications, enabling analysis of genomic, epigenomic and proteomic information quickly and at a low cost.

Since 2003, BioNanomatrix has generated USD 107 million (over EUR 80 million) from seven rounds of funding involving eight private investors. The most recent (Nov 2014) was USD 53 million (c EUR 40 million) with Legend Capital and Novartis Venture Fund. Other investors include Battelle Ventures, Domain Associates, Legend Capital, Novartis Venture Fund, Federated Kaufmann, Monashee Investment Management, and Gund Investment Corporation.

The company is using the funding to expand its commercialisation efforts, develop a next-generation version of its Irys system, and grow its diagnostics capability. Approximately 70% of the employees are involved in R&D (140 out of 200) as of 2014. It also spends nearly 85% of its annual revenue on R&D. So far, 32 institutions in the U.S., Europe and Asia Pacific use 34 Irys systems. These include: the US National Cancer Institute (NCI), US National Institutes of Health (NIH), the Wellcome Trust Sanger Institute, the Broad Institute of MIT and Harvard, BGI, the Garvan Institute, the Salk Institute, and the McDonnell Genome Institute of Washington University.

To leverage the capabilities of cloud computing, DNAnexus Inc. and BioNano Genomics Inc. entered (Oct 2015) into a collaboration that offers access to BioNano's genome analysis algorithms and pipeline (IrysSolve®) on the DNAnexus Cloud Genomics Platform.

[349] www.bionanogenomics.com



NanoAnalyser Technology

10.4.3 Ferrofluids

Ferrofluids[350] are colloidal suspensions of iron-containing magnetic particles (e.g. hematite, magnetite) with typical dimensions of about 10 nm dispersed in a liquid carrier (usually an organic solvent or water). The magnetic particles are coated to avoid agglomeration.

Ferrofluids have been in commercial use since the 1970 in electronic devices such as hard disc data storage devices (where they are used to form liquid seals around the spinning drive shafts). More than 90% of all personal computer hard drives are reported to be equipped with ferrofluid seals[351].

Ferrofluids usually do not retain their magnetisation in the absence of an externally applied field and thus are often classified as "super-paramagnets" rather than 'ferromagnets'[352].

A FERROFLUIDS FOR CANCER TREATMENT

Ferrofluids are being used in an experimental cancer treatment called 'targeted magnetic hyperthermia'. This process takes advantage of the ability of the nanoparticles to convert electromagnetic energy into thermal energy or heat. In this treatment, a ferrofluid is injected into a target tissue, usually a cancerous tumour. An oscillating magnetic field is focused on the location, allowing the ferrofluid to vibrate. The vibration increases the thermal energy at a frequency that does heat the surrounding water. Thus the ferrofluid can reach a temperature that kills the desired cells without damaging surrounding tissue[353].

The NanoTherm™ ferrofluid by MagForce AG[354] (Berlin, Germany) contains iron oxide nanoparticles with an aminosilane coating suspended in water. Despite having an average diameter of just 15

[350] Scherer C, Figueiredo Neto AM (2005), Ferrofluids: Properties and Applications. Brazilian Journal of Physics 35 (3A): 718
[351] BCC Research (2014), Nanotechnology, a realistic market assessment.
[352] Voit, W et al. (2001), Magnetic behaviour of coated superparamagnetic iron oxide nanoparticles in ferrofluids. MRS Proceedings 676 (2001)
[353] Scherer, C, Figueiredo Neto, AM (2005), Ferrofluids: Properties and Applications. Brazilian Journal of Physics 35 (3A): 724.
[354] www.magforce.de/

nanometres, the nanoparticles possess strong magnetic characteristics (super-paramagnetism).

NanoTherm™ therapy is being used for the local treatment of solid tumours. The method is based on the principle of introducing magnetic nanoparticles directly into a tumour and activating the particles using a magnetic field that changes its polarity up to 100,000 times per second, thereby generating heat. Depending on the duration of treatment and the temperatures achieved, the tumour cells are either irreparably damaged or sensitised for additional chemo- or radio-therapy.

B FERROFLUIDS FOR OTHER DISEASES

Superparamagnetic particles have been extensively used in diagnostics and other research applications for the purification of cells and biomolecules, such as antibodies, nucleic acids, and polypeptides. Separation of the nanoparticles is easy due to their magnetic properties and their use is suitable for automation. When coated with recognition molecules, magnetic microspheres are ideal for the efficient capture and separation of targets. Unwanted sample constituents may be washed away following a simple magnetic separation step.

Bangs Laboratories, Inc.[355] (Fishers, IN, USA) supplies uniform polymeric, silica, and super-paramagnetic microsphere products for diagnostic, research, and flow cytometry applications in the United States and internationally. Its three product lines of magnetic beads work across a wide range of applications in the life sciences, from cell separations and immunoassays to suspension arrays and flow cytometry.

MARKET DATA AND FORECASTS

Global consumption of oxide nanoparticles used in ferrofluids was about 5.2 metric tons with a value of USD 1.5 million in 2013. This figure is forecast to rise to USD 1.7 million in 2019 (CAGR 2.5%, 2014-2019). The bulk of these ferrofluids is used in manufacturing loudspeakers and hard disk drives[356].

There is no data currently available on the global consumption of ferrofluids for medical applications.

10.4.4 MRI contrast agents

Although magnetic resonance imaging (MRI) was initially hoped to provide a means of making definitive diagnoses noninvasively, it has been found that the addition of contrast agents in many cases improves sensitivity and/or specificity. MRI contrast agents, amongst which nanomaterials-based contrast agents, have therefore become an indispensable part of modern MRI scanning. Nanoparticles are also being used to enhance imaging techniques[357].

MRI CONTRAST AGENTS FOR CANCER TREATMENT

Magnetic contrast agents have been applied to scanning for cancers in areas including the liver and pancreas. They typically use nanoparticles of iron or gadolinium.

Two types of iron oxide contrast agents exist: superparamagnetic iron oxide (SPIO) and ultra-small superparamagnetic iron oxide (USPIO). These contrast agents consist of suspended colloids of iron oxide nanoparticles and when injected during imaging reduce the T2 signals of absorbing tissues[358]. The iron oxide nanoparticles are coated with an inert material, such as dextran or starch, which reduces absorption (and thus toxicity from the iron), and also helps to suspend the particles in solution. Both SPIO and USPIO contrast agents have been used successfully in some instances for liver tumour imaging enhancement.

Ferumoxsil is a silicone-coated superparamagnetic iron oxide that has been used in MRI scanning. Marketed in Europe as Lumirem® by Guerbet S.A.[359] and in the US as Gastromark® by Mallinckrodt, ferumoxsil is a nanoparticle-based MRI contrast agent that was used to distinguish the loops of the bowel from other abdominal structures and physiology. It was approved by the FDA in 1996. When Lumirem® is ingested, it flows through and darkens the stomach and the small intestine in 30 to 45 minutes. By more clearly identifying the intestinal loops, Lumirem® improves visualisation of adjacent abdominal tissues such as the pancreas. Additionally, in Europe Lumirem® was approved

[355] www.bangslabs.com
[356] BCC Research (2014), Nanotechnology, a realistic market assessment. pp. 119-120
[357] http://radiopaedia.org/articles/mri-contrast-agents
[358] Nakamura, H et al. (2000), Tumor-detecting capacity and clinical usefulness of SPIO-MRI in patients with hepatocellular carcinoma. Journal of Gastroenterology 35 (11): 849–55.
[359] www.guerbet.com/

for rectal administration to delineate the lower intestinal system.

Although SPIOs and USPIOs have been approved for use, it appears that those above and four other contrast agents identified (and listed in the Annex) are no longer available. The reason behind the withdrawals is a combination of low demand and high prices (unless otherwise specified below):

- Gastromark has been withdrawn in the US and no longer appears on the Guerbet web site;
- Feridex I.V. (also known as Endorem and ferumoxides) was discontinued by AMAG Pharma in November 2008[360];
- Resovist (also known as Cliavist) by Bayer Pharma AG[361] was approved for the European market in 2001, but production was abandoned in 2009[362];
- Guerbet withdrew the marketing authorisation application for Sinerem (also known as Combidex) in the USA in 2007[363];
- Takeda Pharma discontinued the development of Clariscan™ (also known as PEG-fero, Feruglose, and NC100150) due to safety concerns[364].

Other nanotechnology-based MRI contrast agents incorporate the paramagnetic material gadolinium, for example, as the contrast agent in MR angiograms and scans for brain tumours. The FDA approved Dotarem® for sale by Guerbet S.A. in 2013. Dotarem is used for MRIs on brain, spine and associated tissues to detect and visualise areas with disruption of the blood brain barrier (BBB) and/or abnormal vascularity.

Iron oxide nanocrystal contrast agents are used only for specific indications (e.g., suspected metastases in the liver) while nonspecific gadolinium-based contrast agents are used for much more general screening[365].

Company snapshot: Guerbet S.A.

Guerbet SA[366], founded in 1926, is a France-based pharmaceutical group specialised in the manufacture and marketing of medical imaging contrast agents destined for diagnostic purposes. It produces medical imaging contrast products for x-ray imaging, magnetic resonance imaging (MRI), ultrasound imaging and for nuclear medicine. The contrast agents are used in the diagnosis of cardio-vascular, inflammatory and neuro-degenerative disorders.

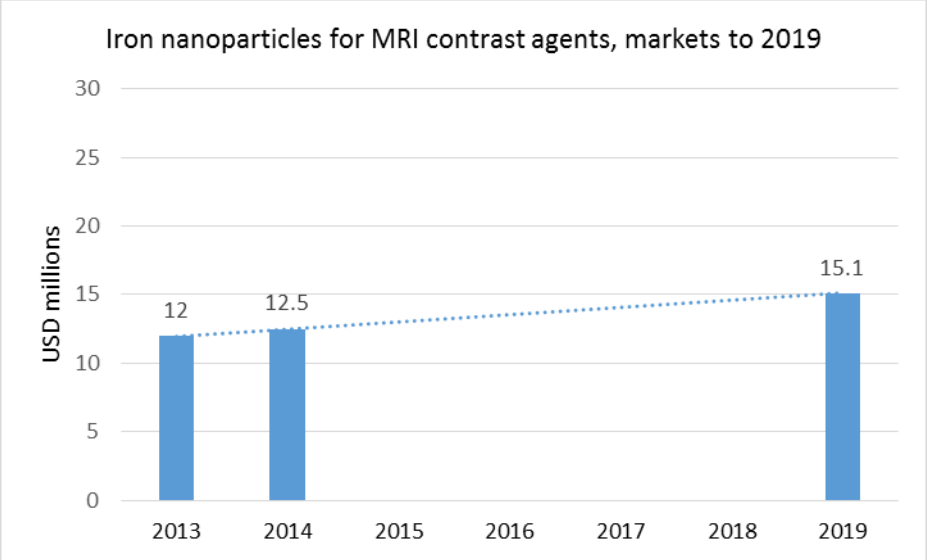
Guerbet's portfolio of products comprises brands, such as Dotarem, Artirem, Xenetix, Hexabrix, Optiray, Oxilan, Telebrix, Lipiodol and Endorem among others. Guerbet SA is also active in the fine chemicals industry through its Simafex subsidiary. The Company operates through its subsidiaries, including Simafex, Medex, SCI KALB, Guerbet LLC, Guerbet Asie Pacifique and Guerbet GmbH, among others.

In 2014, Guerbet realised sales of EUR 409 million and a net income of EUR 26.1 million. It had a total workforce of 1,461 employees at the end of December 2014.

MARKET DATA AND FORECASTS

The global consumption of iron oxide nanoparticles as MRI contrast agents was estimated to be USD 12 million in 2013. The market for iron oxide MRI contrast agents has grown more slowly in the past than the MRI contrast agent market as a whole (at a CAGR of about 9% versus 13%)[367] reflecting the issues of cost and demand mentioned above. The figure below presents the present and future market development.

[360] http://www.mr-tip.com/serv1.php?type=db1&dbs=Feridex
[361] https://pharma.bayer.com
[362] Resovist® competed with gadolinium based Primovist™, the other liver imaging agent of Bayer Schering Pharma AG. Due to this reason, the production of Resovist® has been abandoned in 2009.
[363] http://www.thefreelibrary.com/AMAG+Pharmaceuticals,+Inc.+Announces+Update+on+Sinerem%28TM%29+in+Europe.-a0172378541
[364] Wang, YJ (2011), Superparamagnetic iron oxide based MRI contrast agents: Current status of clinical application, Quant Imaging Med Surg. 2011 Dec; 1(1): 37
[365] Ibid
[366] http://www.guerbet.com/en/en.html
[367] BCC Research (2014), Nanotechnology, a realistic market assessment, p.127



Source: BCC Research, 2014

Figure 10-7: Market trend for iron nanoparticles for MRI contrast agents to 2019

While iron nanoparticle contrast agents are currently experiencing problems of cost and demand relative to other agents, their use may increase overall, although at a slower rate than the contrast agent market as a whole (e.g., at a CAGR of 3.9%). The forecast is for a CAGR of 5% from 2014 through 2019[368]. There is a pipeline of new MRI contrast agents that is slow in obtaining regulatory approval.

Case study: MRI contrast agents: Endomag

The story of Endomag starts in 2003 when the UK Department of Trade and Industry (now Department for Business, Innovation and Skills) funded two academics from University College London (UCL) and University of Houston through the UK/Texas Collaborative Initiative in Bioscience. A grant of USD 250k was provided to Professor Quentin Pankhurst (UCL) and Professor Audrius Brazdeikis (University of Houston) to explore the market for cancer diagnosis on the basis of their expertise on magnetometry (University of Houston) and magnetic nanoparticles (UCL); this was the opportunity to identify the needs of surgeons for alternative cancer diagnosis tools (e.g. magnetic nanoparticle-based localisation) when nuclear medicine facilities were not available.

Endomag was founded as Endomagnetics Ltd in 2007, with a patent for a magnetic susceptometry instrument using liquid nitrogen cooling licensed to the company; at this point a royalty agreement was put in place between Endomag and the American and British universities.

At that time, Endomag was only developing the cryogenic instrument (called Sentimag) and did not control the manufacture of the magnetic nanoparticles.

In 2008, the Technology Strategy Board – Technology for Health Programme of the UK Knowledge Transfer Network (now Innovate UK) funded the development of a non-cryogenic instrument with a grant of STG 398,000 which required 50% matched funding. The matched funding was completed by venture capital supplied by UCL Business, and two other London-based seed funds totalling STG 353,000.

In 2010, Endomag hired its first employee and raised another STG 350,000, then obtained the European CE certification for its device, Sentimag. In the same time, the company developed the other side of the business and formulated its own magnetic nanoparticles, called Sienna+. In 2011, Sienna+ were the first magnetic nanoparticles[369] to be approved as medical devices in the European Union (class IIa). A similar process is underway in the US where the

[368] Ibid
[369] Dextran coated superparamagnetic iron oxide particles, http://www.sysmex-lifescience.com/Sienna-343-2.html

company is expecting FDA approval in 2017.

2011 marked the end of the 'start-up phase'. The company then had to prove the efficacy of the product to the potential customers; hence a multi-site trial (in the UK and in the Netherlands) started in 2012 preceding a commercial launch in November 2012.

Endomag revenues have been growing since then: in 2013, the company's revenue was of STG 545,000 to the year ended April 30th. Revenues doubled to STG 1.02 million for the financial year 2014 and reached STG 2.58 million in 2015.

Sentimag and Sienna+ are now sold in 18 European countries plus Australia and New Zealand and Endomag is looking at markets in the Middle-East and Africa. Over 7 500 patients have now been treated with the Sienna+ magnetic nanoparticles, and over 250 Sentimag devices have now been put in use.

10.4.5 Surface disinfectants

SURFACE DISINFECTANTS FOR MULTIPLE APPLICATIONS

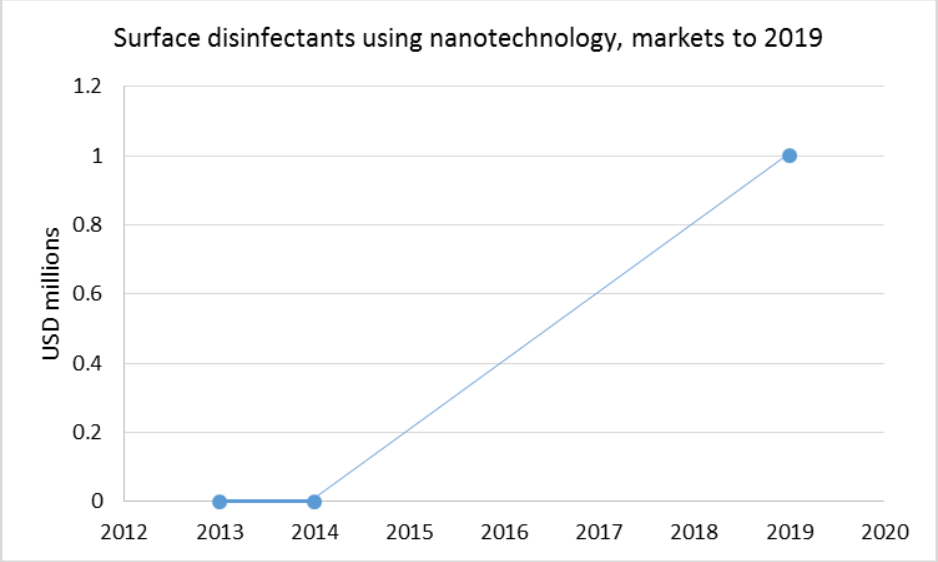
Nanoparticles of silver have long been promoted as having antimicrobial, antibacterial, antifungal, anti-viral and anti-inflammatory properties[370]. A search for products identifies socks, towels and other textiles; brushes, combs, hair straighteners and other beauty products; air purifiers; toothbrushes; pet products; table- and kitchen-ware; taps; binoculars; baby prams and toys, to name but a few[371]. In terms of medical and health applications, surface disinfectants are being marketed (see later also for anti-microbial dressings), some of which are the following:

- Nano Union[372] (Kiev, Ukraine) has introduced SumerSil®, a surface disinfectant based on colloidal silver and copper nanoparticles[373]. Its marketed properties include being active for 200 days in killing staphylococci, streptococci, salmonella, viruses and mould fungi as well as agents of parasitic diseases. In terms of US EPA parameters of toxicity, it is a safe substance (class 4, practically non-toxic and not an irritant).
- A similar product is Nanosept® by Nanobakt kft[374] (Budapest, Hungary). Nanosetp's antimicrobial effects are based on nanosilver. Antibacterial effects of Nanosept® are maintained after the disintegration of hydrogen peroxide of which a small amount is present in the product. This environment friendly nano silver detergent does not contain any chlorine, therefore, it is not toxic, and it does not pollute the environment as opposed to the disinfectants prepared with chlorine which are available in the market[375].
- EnviroSystems[376] (Mooresville, NC, USA) introduced a nanoemulsion formulation of the biocide parachlorometaxylenol (PCMX) under the name EnviroTru in 2002. Nanospheres of oil droplets are suspended in water to create a nanoemulsion with minute amounts the active ingredient, PCMX. The nanospheres carry surface charges that penetrate the surface charges on the membranes of microorganisms. EnviroTru is safe for people, animals and the environment (class 4, practically non-toxic and not an irritant) as it shows no toxicity toward the cells of higher animals.

MARKET DATA AND FORECASTS

It is estimated that global sales of surfaces disinfectants will emerge and will grow, reaching a value in 2019 of USD 1.0 million[377].

[370] http://ehp.niehs.nih.gov/120-a386/; http://www.sciencedirect.com/science/article/pii/S1549963406003467
[371] Search on http://www.nanotechproject.org/ 26 November 2015.
[372] http://www.nanounion.com.ua/files/uploads/text/sumersil-en-e-mail.pdf
[373] Nano Union, Sumersil product Information folder
[374] nanobakt.hu
[375] http://nanosept.hu/en/mi_a_nanosept.html
[376] envirosi.com
[377] BCC Research (2014), Nanotechnology, a realistic market assessment. p.128



Source: BCC Research, 2014

Figure 10-8: Market for surface disinfectants using nanotechnology, to 2019

10.4.6 Proteomic applications

Proteomics is a systematic, high-throughput approach to analyse protein expression of a cell or an organism. Typical results of proteomics studies are inventories of the protein content of differentially expressed proteins across multiple conditions and provide a snapshot of the cell in action. Proteins such as insulin have dimensions of less than ten nanometres (1-3 nm for insulin).

Proteomics technology uses aptamers. Aptamers[378] are single-stranded DNA or RNA molecules that can bind to targets including proteins (and peptides) with high affinity and specificity. They are used as sensors, and therapeutic tools, and to regulate cellular processes, as well as to guide drugs to specific cellular targets. Aptamers have been selected for targets which have a suspected or verified role in diseases in the brain, eyes and kidneys as well as in arthritis, inflammatory, cardiovascular and autoimmune diseases. Whereas antibodies have the ability to specifically recognise tumour cell markers, their large size and immunogenicity often limit their pharmacological value. Aptamers are new promising alternatives to antibodies in diagnostics[379].

PROTEOMICS FOR MANY DIAGNOSTIC APPLICATIONS

SomaLogic Inc.[380] (Boulder, CO, USA) has commercialised aptamer arrays for use in proteomics applications. The SOMAscan TM assay is a highly multiplexed, sensitive, quantitative, and reproducible proteomic tool for the discovery of biomarkers for drug discovery, pre-clinical and clinical drug development, and for clinical diagnostics, across a wide range of diseases and conditions. The SOMAscan assay measures 1,310 protein analytes in as little as 150 microlitres of serum, plasma or cerebrospinal fluid, or equally small amounts of a variety of other biological material. SomaLogic's technology uses photoaptamers, a special type of aptamer assembled into arrays so that large numbers of proteins can be measured simultaneously.

LC Sciences[381] (Houston, TX, USA) provides aptamer microarray services using a novel µParaflo® technology, a list of aptamer sequences, and sequence design software. The aptamer microarrays are applied for protein bindings, drug candidate screening, and biosensor engineering. The protein assay is performed on a µParaflo® biochip with microfluidic µParaflo® technology.

[378] http://www.basepairbio.com/research-and-publications/what-is-an-aptamer-2/
[379] Hjalmarsson K et al. (2004), Aptamers - Future tools for diagnostics and therapy, Swedish defence Agency, FOI-R—1216—SE, p. 19
[380] www.somalogic.com/
[381] http://www.lcsciences.com/

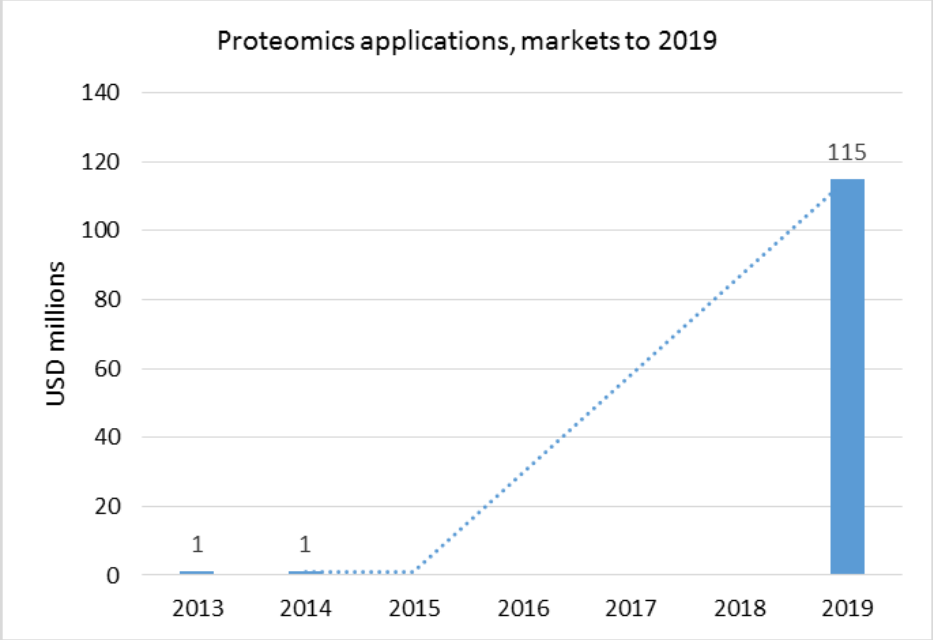
Company snapshot: Proteomics applications: LC SCIENCES[382]

LC Sciences a genomics and proteomics company, provides oligonucleotide and peptide microarray products for nucleic acid and protein-profiling, biomarker-screening, drug screening, and the development of diagnostic-devices. Its products include PicoArray parallel synthesis of DNA oligonucleotides for multiplex applications of library construction, DNA mutagenesis, and DNA synthesis; and array products based on RNA oligonucleotides, oligonucleotide analogues, peptides, and peptide analogues. LC Sciences, LLC was incorporated in 2004 and is based in Houston. LC Sciences generated a revenue of USD 110,000 in 2014.

MARKET DATA AND FORECASTS

The market for protein arrays (which is also the target market for aptamer arrays) is estimated to have been USD 1.7 billion in 2013 and to be growing at a CAGR of 30%, reaching USD 2.2 billion in 2014 and USD 8.2 billion by 2019.

It is difficult to predict with any certainty what share of this market might be captured by the new aptamer arrays. However, another nanotechnology used in proteomics, nano-high-performance liquid chromatography or nano-HPLC, offers a potential benchmark for assessing the potential market for aptamer arrays. Nano-HPLC systems are a subsegment of the capillary HPLC market, consisting of capillary HPLC instruments that have tubes with an inside diametre of less than 100 nm. BCC Research estimates that nanoscale HPLC instruments had captured between 15% and 25% of the capillary HPLC market within five years of their commercialisation. Applying similar percentages to the protein array market implies that aptamer arrays, if commercialised, might capture a market valued between USD 1.2 billion and USD 2.1 billion from conventional protein arrays by 2019. In view of the aptamer array technology's newness, BCC Research believes that the actual number will be closer to the low end of this range[383].



Source: BCC Research, 2014

Figure 10-9: Proteomics applications, markets to 2019

10.4.7 Synthetic bone and tooth enamel

Bone is a bio-composite material of which the major constituent (60-70% of bone by weight) is a complex mineral mixture of calcium and phosphate in the form of tri-calcium phosphate, also called

[382] Ibid
[383] BCC Research (2014), Nanotechnology, a realistic market assessment. pp. 134-135

hydroxyapatite or hydroxylapatite. Bone also contains proteins (20-30%) and water (10%). The dimensions of the mineral and organic constituents of bone are on the nanometre scale[384].

Hydroxyapatite nanoparticles for use as bone replacement material are commercially available in the form of bone cements used following bone fractures, during hip prosthesis revision surgery, in acetabulum reconstruction, in osteotomies, to fill cages in spinal column surgery, and to fill bone defects in children[385]. Typically, the hydroxyapatite is mixed with a biodegradable substance (e.g. polymer) which gradually leaches out leaving the bone to grow in to and absorb the hydroxyapatite.

Hydroxyapatite (in a carbonated and calcium-deficient form) is also the main mineral of which dental enamel and dentin are composed. Hydroxyapatite nanoparticles are also used in replacement tooth enamel due to their biocompatibility and their white colour.

A SYNTHETIC BONE APPLICATIONS

Orthovita Inc. commercialised the first nano-particulate synthetic bone substitute, VITOSS® bone void filler. Vitoss was approved by the FDA in 2003[386]. In 2011, Orthovita was acquired by Stryker Corp.[387] (Kalamazoo, MI., USA), which now manufactures and markets VITOSS®. VITOSS® contains hydroxyapatite[388] nanoparticles with a diameter of ~100 nm. It is engineered to resemble human cancellous bone[389] in porosity and structure. Higher porosity and larger surface area, compared to conventional tri-calcium phosphate, facilitates faster and increased bio-resorption and vascular invasion[390].

Ostim® by Heraeus Kulzer GmbH[391] (Hanau, Germany) was introduced to market in 2003. Ostim® is synthetic nano-crystalline hydroxyapatite in the form of an aqueous watery paste that can be used to fill bone defects or to build up bony structures in the region of the jaws. Ostim is osteo-conductive, facilitating bone growth. It can act as a scaffolding for the new bone, resorbed during the healing process. At first, the natural bone grows into the hydroxyapatite, in an osseous interweave; finally, the natural bone completely absorbs the new material and replaces it with natural bone[392].

In May 2005, Angstrom Medica, Inc. (Woburn, Mass., USA) obtained FDA approval to commercialise their engineered synthetic bone product NanOss™. The material is composed of hydroxyapatite nanocrystals, sized and shaped like natural bone crystals but with the strength of stainless steel[393]. NanOss finds applications where natural bone is damaged or removed, such as in the treatment of fractures and also as a replacement for allograft (donor bone) and metallic medical devices in the areas of spine and sports medicine. In 2007, Angstrom Medica was acquired by Pioneer Surgical Technology which continues to sell NanOss™[394].

Shanghai Rebone Biomaterials Co.[395] (China) has developed in 1998 calcium phosphate cement (CPC), a kind of novel material for bone defect repair and dental root canal filling funded by National Hi-tech Developing Program (863 plan). Characterised with easily shaping and handling, excellent biocompatibility and osteo-conductivity, and suitable biodegradability, this ideal novel bone substitute can be applied extensively into such many fields as orthopaedics, neurosurgery, plastic surgery, and dentistry. CPC obtained the production approval from State Drug Administration at Dec. 2000.

B TOOTH ENAMEL APPLICATIONS

Hydroxyapatite (HA) is the main component of enamel, which gives an appearance of bright white

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[384] Rho JY et al. (1998), Mechanical properties and the hierarchical structure of bone. Med. Eng. Phys. (20): 92-102
[385] Szpalski M, Gunzburg R (2002). Applications of calcium phosphate-based cancellous bone void fillers in trauma surgery. Orthopaedics 25: pp601-609
[386] Etheridge ML, et al (2014), The big picture on nanomedicine: the state of investigational and approved nanomedicine products. Nanomedicine: Nanotechnology, Biology, and Medicine 9 (2013): 9
[387] www.stryker.com
[388] Here being in the form of β-tri-calcium phosphate
[389] Also known as spongy bone, cancellous bone is found at the ends of long bones such as the thigh bone, as well as in the pelvic bones, ribs, skull, and the vertebrae of the spinal column.
[390] Szpalski M, Gunzburg R (2002). Applications of calcium phosphate-based cancellous bone void fillers in trauma surgery. Orthopaedics 25: 601-609
[391] www.heraeus-kulzer.de
[392] Heraeus, Nanocrystalline bone grafting material Ready to use, product information.
[393] Indian J Surg. 2013 Dec; 75(6): 485–492
[394] www.pioneersurgical.com
[395] www.rebone.com/en/

and eliminates the diffuse reflectivity of light by closing the small pores of the enamel surface[396]. The nano-hydroxyapatite is a revolutionary material with a wide use in dentistry. With regard to restorative and preventive fields, nano-hydroxyapatite has remarkable re-mineralising effects on initial lesions of enamel, certainly higher than traditional fluorides used until now for this purpose. Nano-hydroxyapatite is, in fact, a better source of free Ca, and this is a key element as regards the remineralisation, the protection against caries and dental erosion[397].

Biomet Inc. (Warsaw, IN, USA) produces a dental implant called NanoTite which deposits nanoscale calcium phosphate crystals to approximately 50% of the implant surface[398].

Company snapshot: Fluidinova SA

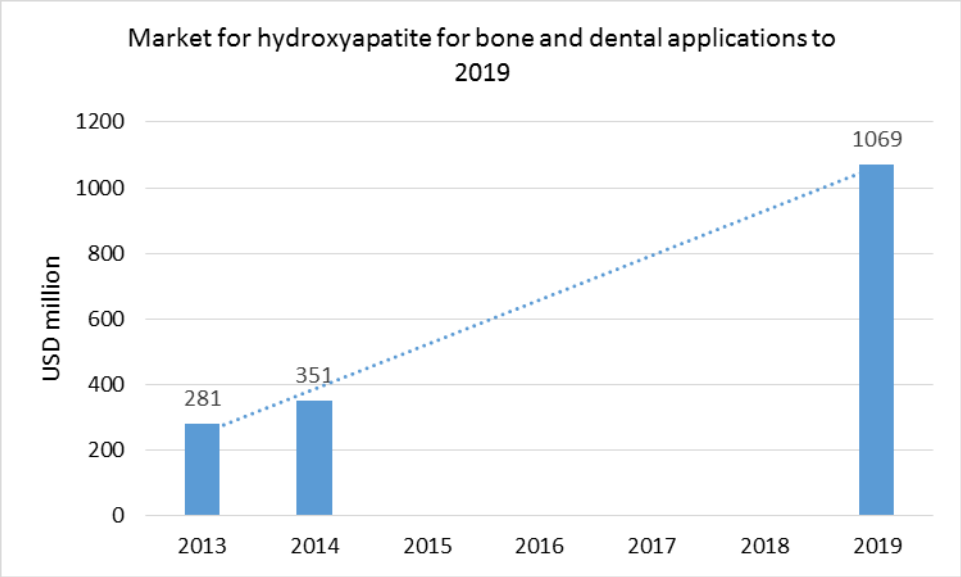
FLUIDINOVA is a specialised manufacturer of synthetic nanocrystalline hydroxyapatite materials commercialised worldwide under the brand name nanoXIM.

Located in the Porto area, Portugal, FLUIDINOVA was created in 2005 as a spin-off from the Faculty of Engineering of the University of Porto. Having computational fluid dynamics as core knowledge base, the team developed a proprietary technology – NETmix - to perform chemical reactions that require perfect mixing at a micro to nanoscale. FLUIDINOVA produces highly pure, single phase nano-hydroxyapatite materials supplied as pastes and powders for the manufacture of personal care products and medical devices and for use in R&D activities and innovative applications.

Currently nanoXIM is incorporated in several FDA approved and CE mark medical devices. Other applications for nanoXIM include chewing gums, cosmetics, drug delivery, pharma and biotech.

MARKET DATA AND FORECASTS

In 2013, total global consumption of nano-particulate calcium phosphate and hydroxyapatite used as bone substitutes or toothpaste ingredients was around 32 tonnes, with a value of USD 280 million. This figure is forecast to reach USD 350 million in 2014 and about USD 1.1 billion by 2019[399].



Source: BCC Research, 2014

Figure 10-10: Market for nano-particulate hydroxyapatite to 2019

[396] Pepla E et al. (2014), Nano-hydroxyapatite and its applications in preventive, restorative and regenerative dentistry: a review of literature. Annali di Stomatologia 2014 Jul-Sep; 5 (3): 108–114
[397] Ibid
[398] http://www.nanopinion.eu/sites/default/files/surgery_implants_and_coatings-april_09.pdf, p3
[399] BCC Research (2014), Nanotechnology, a realistic market assessment. p.119

10.4.8 Transfection reagents

Transfection is the introduction of foreign DNA into bacterial and/or mammalian cells and is used to investigate gene function and gene expression for the advancement of basic cellular research, drug discovery and target validation. There are many different protocols and techniques depending on the application. These include DEAE-dextran, calcium phosphate, electroporation, liposomes, viral vectors, non-liposomal lipids and activated dendrimers[400]. Dendrimers are highly branched, star-shaped macromolecules with nanometre-scale dimensions.

DENDRIMER-BASED TRANSFECTION REAGENTS

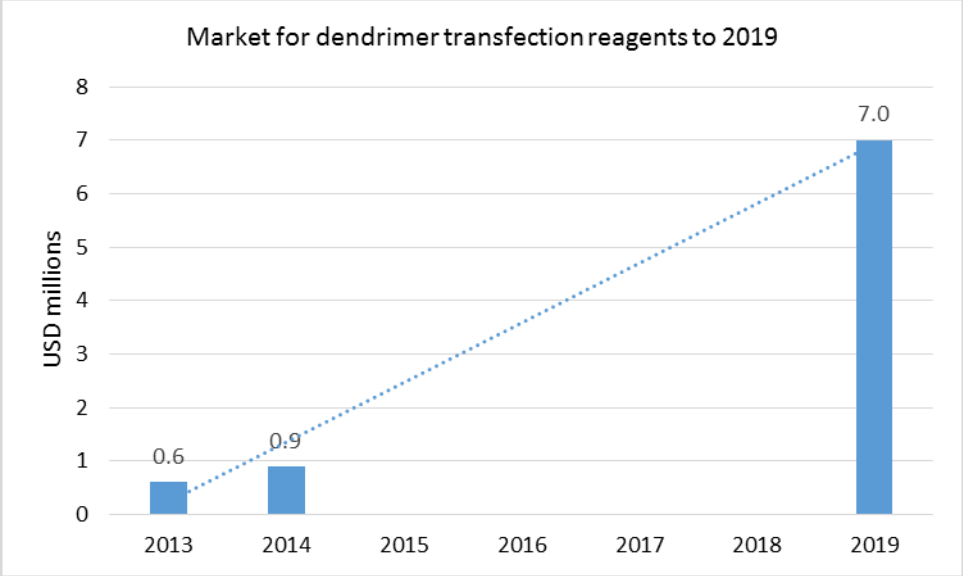
Qiagen N.V. (Venlo, Netherlands) was the first company to develop and market a dendrimer-based transfection reagent, called SuperFect. Other firms have since introduced dendrimer transfection agents of their own. The SuperFect Transfection Reagent is used in molecular biology applications and consists of activated-dendrimer molecules with a defined spherical architecture. Branches radiate from a central core and terminate at charged amino groups which can then interact with negatively charged phosphate groups of nucleic acids. SuperFect Reagent assembles the DNA into compact structures that bind to the cell surface and are absorbed into the cell, buffering the pH and ensuring stability of the SuperFect–DNA complexes. Due to highly controlled chemical synthesis, the activated-dendrimer molecules in SuperFect Reagent have a precise size and a defined shape. This ensures consistent transfection-complex formation and reproducible transfection results[401].

> ***Company snapshot: Qiagen NV***
>
> *QIAGEN N.V. was founded in 1996 and is headquartered in Venlo, the Netherlands. It is a leading global provider of sample and assay technologies. Sample technologies are used to isolate and process DNA, RNA, and proteins from biological samples such as blood or tissue. Assay technologies are used to make such isolated biomolecules, such as the DNA of a specific virus, visible for subsequent analysis.*
>
> *The company serves molecular diagnostics, applied testing, pharma, and academic customers. It has collaboration agreements with Astellas Pharma Inc., AstraZeneca PLC, Eli Lilly and Company, Exosome Diagnostics Inc., and Novartis AG.*
>
> *In 2014 QIAGEN N.V. employed over 4,300 people and generated revenue of EUR 1.29 billion. The Company's main competitors are: Sigma-Aldrich Corp., Roche Diagnostics GmbH, Promega Corp., EMD Millipore, Macherey-Nagel GmbH, Thermo Fisher, Hologic, Inc., Abbott, Siemens and Cepheid*.

MARKET DATA AND FORECASTS

Growth is expected in the overall market for transfection reagents as well as in the share of dendrimer-based reagents in that market. The global market for transfection reagents was worth an estimated USD 425 million in 2013, increasing at a CAGR of about 10%. Thus, the total market for transfection reagents is forecast to be worth USD 0.47 billion in 2014 and USD 0.7 billion by 2019. If dendrimer-based transfection reagents achieve a 10% share of the transfection reagent market by 2019, they will reach sales of c. USD 70 million. At an estimated 10% of total transfection reagent cost, related consumption of dendrimers should be worth about USD 7 million in 2019[402].

[400] http://www.bio-rad.com/de-at/applications-technologies/transfection
[401] http://californiananoeconomy.org/products/superfect-transfection-reagent
[402] BCC Research (2014), Nanotechnology, a realistic market assessment. p.125



Source: BCC Research, 2014

Figure 10-11: Market for dendrimer transfection reagents to 2019

10.4.9 Nano-porous membranes

Molecular transport controlled at the nanometre-scale using membranes offers great potential for high selectivity and high throughput. Many applications, including protein separation and purification, biomolecule detection and drug delivery, are now being realised using nanoscale pore structures that can provide high selectivity based on specific molecular characteristics[403]. In the last 35 years or so, nano-porous membranes with a reasonably uniform pore-size distribution have become commercially available. Membranes with nanometre-scale features have many applications, such as in optics, electronics, catalysis, selective molecule separation, filtration and purification, bio-sensing and single-molecule detection[404].

Organic polymeric nano-porous membranes have been used for dialysis filters since the late 1990's. Notable examples are Polysulfone® or Helixone® by Fresenius SE & Co KGaA[405] (Bad Homburg, Germany) and the Polyflux® 210H by Gambro AB (Lund, Sweden)[406].

Further health application areas for nano-porous membranes can be found in blood gas analysers. Epigem Ltd.[407] (Redcar, UK) and Radiometre Medical aps[408] (Brønshøj, Denmark) have recently developed sensor platforms for blood analysis on the basis of nano-porous membranes.

Company snapshot: Fresenius SE & Co KGaA[409]

Fresenius SE & Co KGaA is a global health care group with products and services for dialysis, in the hospital and for the medical care of patients at home. It was founded by Eduard Fresenius in October 1912 and is headquartered in Bad Homburg, Germany. The Company sells dialysis, infusion, transfusion, and diagnostics equipment and systems, blood separators and plasma and hemofilters, nutritional liquids, and solid and liquid pharmaceuticals. In 2014 Fresenius SE & Co KGaA employed over 210,000 people and generated revenue of over EUR 23 billion. It operates through the following: Fresenius Medical Care, Fresenius Kabi, Fresenius Helios, and Fresenius Vamed. The Fresenius Medical Care segment provides dialysis products and services for patients with chronic kidney failure and realised sales of almost EUR 12 billion in 2014.

[403] Stroeve P, Nazar N (2011), Biotechnical and other applications of nano-porous membranes, Trends in Biotechnology 879: 1
[404] Ibid
[405] www.fresenius.de/
[406] Gambro AB is since 2012 part of Baxter
[407] epigem.co.uk
[408] www.radiometer.com
[409] http://www.fresenius.com/documents/GB_US_GAAP_2014_englisch.pdf

MARKET DATA AND FORECASTS

While there is no available market data on the specific use of nano-porous membranes in medical applications, the table below shows global market estimates for membranes as a whole for water filtration and refinery separation. Nano-porous thin film membranes include membranes used in water filtration applications (e.g. Dow Chemical's Filmtec) and refinery separation membranes.

Water filtration membranes are expected to grow with a CAGR of 15.0 % to reach global sales of USD 925 million in 2019. Although it is difficult to quantify the potential global market for nano-porous membranes in the refinery industry, it is estimated that global consumption in 2019 will be USD 100 milion[410].

Table 10-4: Global consumption of nano-porous thin film membranes to 2019

	USD Million			CAGR% 2014-19
	2013	2014	2019	
Water filtration membranes	400.0	460.0	925.0	15.0
Refinery separation membranes	Neg.*	Neg.*	100.0	–
Total	400.0	460.0	1,025.0	17.4

Source: BCC Research, 2014

10.4.10 Antimicrobial applications

Silver has long been used to fight infection. It interrupts the bacterial cell's ability to form the chemical bonds essential to its survival. These bonds produce the cell's physical structure so when the bacteria meets silver it literally falls apart. Wound dressings containing silver have been an important aspect of healthcare for more than a century; soldiers in World War I relied heavily upon such dressings.

ANTIMICROBIAL DRESSINGS FOR HEALTH

Today, many consumer healthcare companies manufacture bandages and ointments that use nanosilver in thin film and coating form as an active ingredient[411] as well as appliances such as catheters.

In 1998, Nucryst Pharmaceuticals (Princeton, NJ, USA) introduced the first commercially available product based on its platform nano-crystalline technology. Nano-crystalline silver (Silcryst) is widely used in dressings for serious wounds and burns.

A product using Silcryst nano-crystalline silver is distributed and marketed by Smith & Nephew plc[412] (London, UK) under the name Acticoat. Acticoat is used in hospitals and burn centres in 30 countries around the world to treat life-threatening burns and serious wounds like pressure ulcers, diabetic foot ulcers and venous stasis ulcers. Since 2001, Smith & Nephew has held exclusive license for the sale of the ACTICOAT dressing portfolio. In 2009, all assets related to Silcryst Technology were acquired by the Advanced Wound Management division of Smith & Nephew plc.

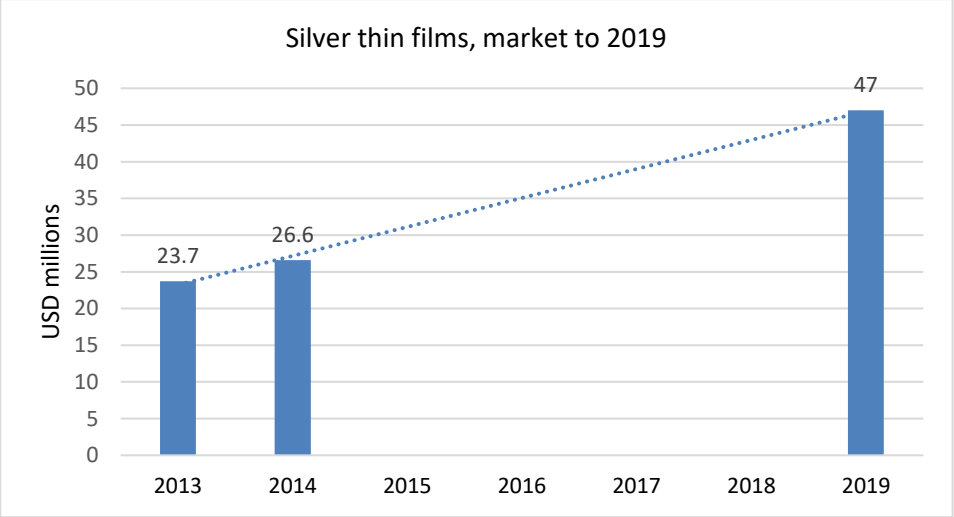
The ON-Q SilverSoaker by Halyard[413] (former Kimberly-Clark Healthcare) in the US and by Braun Melsungen AG[414] (Melsungen, Germany) in Europe is a catheter treated with a specially formulated antimicrobial silver agent (SilvaGard), that can destroy or inhibit the growth of micro-organisms on the inner and outer surface of the catheter. SilvaGard has been initially developed by AcryMed Inc. as a silver nanoparticle antimicrobial coating that protects against the formation of infection-causing biofilm. AcryMed Inc was acquired by I-Flow in 2007 which was in turn taken over by Kimberly-Clark Corp. (Alpharetta, Georgia, USA) in 2009.

MARKET DATA AND FORECASTS

The estimated global consumption of silver thin film materials was USD 23.7 million in 2013. With an expected CAGR of 12.1 %, global sales volumes should reach USD 16.6 million in 2014 and USD

[410] BCC Research (2014), Nanotechnology, a realistic market assessment. p.151
[411] https://www.silverinstitute.org/site/silver-in-technology/silver-in-medicine/bandages/
[412] www.smith-nephew.com
[413] www.halyardhealth.com
[414] www.bbraun.com

47.0 million in 2019[415].



Source: BCC Research, 2014

Figure 10-12: Markets for silver thin films to 2019

Case study: Antimicrobials: Smith & Nephew

Smith & Nephew plc (established in 1896) is a British-based multinational medical equipment manufacturing company with focus on arthroscopy products, advanced wound management products, trauma and clinical therapy products and orthopaedic reconstruction products.

Smith & Nephew invested 5.1% (i.e. USD 235 million, EUR 176 million) of its 2014 revenues (USD 4.6 billion, EUR 3.5 billion) in R&D. The nanotechnology-specific R&D investment range is 8-10% of that annual R&D expenditure (EUR 14-18 million).

The company has over 100 R&D employees globally that work in nanotechnology-related activities (materials research, testing, device integration, formulation etc.). Some of the other notable recent R&D programmes are:

- JOURNEY II BCS: a major new knee platform
- HEALICOIL REGENESORB Suture Anchor, the first sports medicine product to use Smith & Nephew's proprietary advanced bio-composite material; and
- DURAFIBER Ag, combining a highly absorbent, gelling fibre dressing with the antimicrobial benefits of silver.

The company is a pioneer in the wound care and management segment and is a leading adopter of nanotechnology in its products. In particular, the Acticoat family consists of dressings which are flexible, absorbent and conformable that provide a barrier to bacterial penetration. The nanocrystalline Silcyst silver on Acticoat dressings is created via a physical vapour deposition process to form a structure with a large accessible surface area. This product alone accounts for 2.3% (USD 106 million, EUR 80 million) of total revenue in 2014.

The company has a patent portfolio of over 5000 patents owing to its wide range of R&D activities across segments. Specifically, linked to Acticoat the innovation is a patent under patent no. US 20040001880.

Smith & Nephew has been active in EU projects including:

- ENDURE (Enhanced Durability Resurfacing Endoprosthesis);
- ANGIOSCAFF, in the first series of biomaterial development and validation projects;
- NANOMINING (Development of new nanocomposites using materials from mining industry).

As part of its overall strategy, Smith & Nephew supports and works with numerous small companies to develop and commercialise new technologies. Some of the notable activities

[415] BCC Research (2014), Nanotechnology, a realistic market assessment, p.153

in this regard are:

- Commercial partner in SWAN-iCare, an EU-funded initiative to bring multidisciplinary European research teams together to deliver a next generation integrated autonomous solution for monitoring and adapting personalised therapy of foot and leg ulcers;
- NASA's TecFusion Open Innovation programme provides the company opportunity to access and support companies developing disruptive technologies (funded by the US federal government);
- Supporting entrepreneurial product development of early-stage medical device companies through the Massachusetts Medical Device Development Centre ('M2D2') New Venture Competition; and
- Through its InVentures programme, Smith & Nephew also welcomes new product concepts from surgeons and bring their ideas to reality.

10.4.11 Drug production and mixing systems

The number of poorly soluble drugs is steadily increasing as drug discovery produces drugs of increasing molecular size. Many are simultaneously poorly soluble in water and in non-aqueous media and hard for the body to absorb. There is therefore an increasing demand for strategies to overcome this problem, leading to new types of drug formulations and carriers[416].

DRUG PRODUCTION THROUGH NANOTECHNOLOGY

The Microfluidizer® by Microfluidics Corp.[417] (Newton, Mass., USA) is making use of the jet-stream principle[418] for the production and mixing of nanoscale drug particles. The Microfluidizer can be used for the production of drug nano-suspensions. However, this technique is not very convenient for large scale production as a large number of cycles (50 to 100 passes) are required for sufficient particle size reduction. This technique is being utilised by SkyePharma Canada Inc. for production of submicron particles of poorly soluble drugs and named it IDD-PTM (In soluble Drug Delivery-Particle technology)[419].

Nanopure® technology, owned and developed by Pharmasol GmbH[420] (Berlin, Germany), is based on the Piston-gap homogenisation in water-reduced mixtures or non-aqueous medium. The development is based on the principle that cavitation occurs in the aqueous phase. The particle suspension has a very high flow velocity when passing the tiny gap of the homogeniser; the static pressure on the water decreases below the vapour pressure of water; the water starts boiling at room temperature leading to the formation of gas bubbles; and at the exit of the gap the gas bubbles implode. The implosion shock waves disintegrate the drug particles to drug nanoparticles. Due to the cavitation principle this process is more efficient the higher the temperature is, i.e. the higher the vapour pressure of water is. Special features of the developed Nanopure technology are that the homogenisation can be performed in a non-aqueous phase or phases with reduced water content[421].

Company snapshot: Microfluidics

The Microfluidics International Corporation designs, manufactures, and distributes high-shear fluid processors for uniform particle size reduction, robust cell disruption, and bottom-up nanoparticle creation. It sells high pressure homogenisers, such as low volume benchtop machines, high pressure pneumatic micro-fluidiser processors, air-driven homogenisers, and high pressure lab homogenisers. The company also provides pilot/production machines, including mobile high-shear fluid processors. In addition, it offers chambers and spare parts, preventive maintenance, product updates, and process and scale-up consulting services. Its products are used in pharmaceutical applications, such as vaccines/adjuvants, cancer therapeutics, antibiotics, injectables, inhalables, anaesthetics, and steroids. Microfluidics International Corporation was formerly known as MFIC Corporation and changed its name to

[416] Radtke M (2001), Pure drug nanoparticles for the formulation of poorly soluble drugs. New Drugs 2001 (3): 62–68.
[417] www.microfluidicscorp.com
[418] Two streams of liquid with high velocity (up to 1000 m/sec) collide frontally under high pressures (up to 1700 bars). The particle size is reduced due to high shear force particle collision and cavitation. Surfactants or phospholipids are required to stabilize the desired particle size.
[419] International Journal of Research in Pharmaceutical and Biomedical Sciences, Vol. 3 (1) Jan – Mar 2012: 409
[420] www.pharmasol-berlin.de
[421] Radtke M. (2001), Pure drug nanoparticles for the formulation of poorly soluble drugs. New Drugs 2001; 3: 62–68.

Microfluidics International Corporation in June 2008. The company was founded in 1983 and is based in Westwood, Massachusetts with an additional office in Worcestershire, United Kingdom. Microfluidics International Corporation operates as a subsidiary of Fluid Management, Inc.

MARKET DATA AND FORECASTS[422]

Devices that use microfluidics technology to produce and mix nano-particulate drugs, such as Microfluidics Corp.'s MMR system, have only recently become available on the market. Microfluidics has sold "beta" versions of its Microfluidics Reaction Technology (MRT) or PureNano system, which incorporates the MMR reactor, to drug manufacturers, but there have been no known commercial sales as of July 2014. By 2019, it is estimated that sales of MMR systems by the company could equal recent sales of the company's macroscale system, USD 8 million.

10.5 Emerging application markets in health through nanotechnology

10.5.1 Aptamer-based molecular imaging agents

Molecular imaging is increasingly able to characterise and quantify (sub)cellular biological processes in intact organisms, processes such as gene expression, protein-protein interaction, cellular metabolism, and signal transduction. It has the potential to quantify these physical and chemical events in three dimensions and over time. Molecular imaging has only been made possible by the enormous advances in imaging probes through technologies such as nanotechnology (increasing accuracy, reliability and throughput) and advances in molecular biology and cell biology[423].

Aptamers having inherently low molecular weight are cleared rapidly from the bloodstream, with a half-life of minutes to hours, mainly through the kidneys. This rapid clearance can be an advantage for in vivo diagnostic imaging. Schering AG is developing a tenascin-binding aptamer for cancer imaging[424]. Aptamer-based imaging has also potential clinical applications in neuropsychiatry, angiogenesis and the monitoring of gene therapy[425].

As of 2014, no aptamer-based molecular imaging agents were available commercially. However, it is forecast that producers will enter the market and capture a potential molecular imaging market of over USD 5 billion by 2019. In general, the market for medical imaging contrast agents is estimated at about 40% the size of the imaging equipment market, so total sales of imaging agents for molecular imaging studies are estimated at USD 2.1 billion in 2019. If aptamer-based imaging agents can capture 10% of this market in 2019, they will be worth USD 210 million. This will depend on competition from established imaging contrast agents and uncertainty regarding the timeline remains[426].

10.5.2 Nanostructured magnetic coatings for medical devices

Some types of implantable medical devices cannot be used in conjunction with MRI scanning (e.g. heart pacemakers, defibrillators, neuro-stimulators and guidewires) as the magnetic field of the MRI scanner may cause unsafe levels of heating of the devices and even induced voltages. Companies are working to delivery safe alternatives.

Biophan Technologies[427] (Pittsford, NY, USA) has reportedly developed a nanostructured magnetic coating for drug-eluting stents and orthopaedic implants designed to provide physicians with greater control over drug delivery than is currently possible with conventional drug-eluting devices. The coating contains nano-magnetic particles that can selectively bind to drugs, then selectively release them when a controlled electromagnetic field at a specific frequency is applied. Multiple drugs can be delivered independently and/or at different times, if the nanoparticles respond selectively to different frequencies.

The market for all types of implantable drug delivery devices is projected to grow from USD 13.5

[422] BCC Research (2014), Nanotechnology, a realistic market assessment. p. 194
[423] Roszek B et al. (2005), Nanotechnology in medical applications: state-of-the-art in materials and devices, RIVM report 265001001/2005, p. 88
[424] http://www.protein.pl/?name=aptamers
[425] INTECH OPEN: Nucleic Acid Aptamers for In Vivo Molecular Imaging
[426] BCC Research (2014), Nanotechnology, a realistic market assessment. p. 136
[427] http://www.biophan.com

billion in 2013 to USD 21.4 billion in 2019. Given the need for extensive clinical testing, nano-coated devices are unlikely to capture a large share of this market in that timeframe. However, even a 1% share of the target market would mean sales of over USD 200 million in 2019, the coating being about 2.5% of the total cost of the implanted device (i.e. a market for the nano-magnetic coatings of USD 5 million in 2019).[428]

10.5.3 Biocompatible coatings for medical devices and implants

Coronary stents in bare metal can induce negative effects (e.g. platelet activation[429]) by shear stress, release of metal ions, and contact to the blood vessel wall, triggering thrombosis (coagulation or clotting of blood in the body). Traditionally, surface coatings on stents are applied to reduce thrombogenicity by lowering blood protein adsorption and thrombocyte aggregation. Applying nano-porous ceramic coatings may even further improve efficient stenting. Currently, several nano-porous ceramic coatings, e.g. aluminium oxide and hydroxyapatite, are being developed at companies such as AlCove Surface GmbH (Gladbeck, Germany), Debiotech SA (Lausanne, Switzerland), and MIV Therapeutics, Inc. (Vancouver, British-Colombia, Canada)[430].

Nano-porous technology is enabling next generation coronary stents that carry drugs or are coated with a semi-permeable barrier[431]. Drug-eluting stents have been in use for over a decade: the sirolimus-eluting Cypher stent was approved and released to the market in 2003. Most recently, in January 2015, the US Food and Drug Authority (FDA) approved Medtronic's Resolute Integrity Zotarolimus-eluting Coronary Stent System, zotarolimus being a drug that prevents the coronary artery from re-narrowing[432]. Nanotechnology is one tool in the development of new and better stents.

Abbott Vascular (Santa Clara, CA, USA) in 2011 received FDA approval for its XIENCE nano™ Everolimus Eluting Coronary Stent System. The XIENCE nano stent is a metal stent with the drug everolimus contained in a polymer thin-film coating on the stent's surface. The XIENCE nano stent is mounted on a folded balloon attached to a catheter delivery system for placement into a coronary artery (blood vessel supplying blood to the heart). The stent is made of a cobalt-chromium metal alloy[433].

MIV Therapeutics[434] (Vancouver, Canada) is developing a stent, called VESTAsync that uses the company's proprietary hydroxyapatite coating, a porous, polymer-free material that can be used to carry and deliver drugs once implanted in the body, or as a passive, protective coating. MIV Therapeutics sees potential for its hydroxyapatite coating with other types of implantable devices; it partnered up with Smith & Nephew in 2007 to work on orthopaedic implants.

Inframat Corp.[435] (Manchester, Conn., USA) is developing nanostructured hydroxyapatite coatings for various prostheses that use a room-temperature electrophoretic deposition process. Research to date has been in an NIH Phase I grant, where Ti_6Al_4V coupons were electrophoretically coated and exposed over several months to simulated body fluids. Animal studies have been proposed in a Phase II submittal to the NIH.

The global market for coronary stents is expected to reach USD 13.5 billion by 2019. The coated and drug-eluting stent segment is forecast to account for 80% of the total stent market, or USD 10.8 billion, by 2019[436]. Even assuming that the newer stents receive FDA and other regulatory approvals, it is difficult to project their actual sales in 2019, particularly in view of the competition from various other coated and drug-eluting stents. As in the case of nano-magnetic-coated drug delivery devices, conservative forecasts are that HAp-coated stents will capture 1% of the coated and drug-eluting

[428] BCC Research (2014), Nanotechnology, a realistic market assessment. p. 164
[429] http://www.platelet-research.org/1/function_acti.htm
[430] Roszek B et al. (2005), Nanotechnology in medical applications: state-of-the-art in materials and devices, RIVM report 265001001/2005, p. 69
[431] Ibid
[432] http://www.medtronic.com/ , http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm345065.htm
[433] http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm257680.htm
[434] http://www.mivtinc.com/
[435] http://www.inframat.com
[436] BCC Research (2014), Nanotechnology, a realistic market assessment. p. 164

stent market by 2019, or USD 108 million[437].

10.5.4 Dental and medical implants

Timplant Ltd.[438] (Ostrava, Czech Republic) introduced the first dental implant system in the world made from nanostructured titanium in 2009 with NANOIMPLANT®. The development of the NANOIMPLANT® implant system and research of nano-titanium properties has been performed in cooperation with Charles University in Prague, the Department of Dentistry of the Medical Faculty in Pilsen and the VSB Technical University of Ostrava (all in the Czech Republic) and with the State Technical Aviation University of Ufa (Russian Federation).

Titanium and its alloys have been widely used as implant materials for orthopaedic applications owing to their excellent wear, corrosion resistance, light weight but strong mechanical and acceptable biocompatibility properties. With a normal lifetime of less than 20 years, with a variety of causes and final separation of the implant from the bone[439], alternatives are needed. One approach is to abandon alloying altogether and to enhance the mechanical properties of pure titanium by nanoscale grain refinement using severe plastic deformation (SPD) processing[440].

Worldwide consumption of titanium for use in orthopaedic implants was USD 220 million in 2013, forecast to rise to USD 295 million in 2019 (a CAGR of 5% from 2014 through 2019) [441]. If nanostructured titanium delivers on its potential to replace half of the conventional titanium and titanium alloys used in medical implants by 2019, assuming the average cost of nanostructured titanium materials for implants is similar to the average cost of currently used medical-grade titanium materials, this would represent a potential market of close to USD 150 million by 2019[442].

10.5.5 Nanocomposite-based bone replacements and cements

As seen previously, bone tissue regeneration is best achieved when the biomaterial can mimic living bone tissue. Since no single type of material can exactly match the composition, structure and properties of natural bone, nanocomposites are the best choice for bone tissue regeneration as they provide a suitable matrix and good biological properties, and can provide for controlled, sequential delivery of multiple growth factors for the different stages of bone tissue regeneration[443].

The nanocomposite material that appears closest to commercialisation in orthopaedic implants for spinal and maxillofacial applications is a porous resorbable silica-calcium phosphate nanocomposite material. A Kentucky startup firm called Ostech tried for several years to commercialise such a nanocomposite, but apparently has since gone out of business. However, there is still significant research interest in silica-calcium phosphate nanocomposite[444].

In the BIOKER (2003-2006) project, funded under the European Commission's GROWTH programme, methods and materials were investigated with the aim to increase the life span of ceramic-ceramic knee and hip orthopaedic implants. Zirconia-toughened alumina nanocomposites were used to form ceramic-ceramic implants with potential life spans of more than 30 years. The project led to the development of a material composed of zirconia nanoparticles distributed uniformly among alumina grains.[445].

Such calcium phosphate/silica nanocomposite bone replacement materials are not yet available commercially as of mid-2014. While the global bone graft market is projected to exceed USD 3 billion by 2019, nanocomposite bone graft materials will compete with natural bone, macroscale artificial bone and nanoparticulate hydroxyapatite implants for a share of this market. It is estimated that all forms of synthetic bone (nanoparticulate as well as nanocomposite) may capture one-third, or at least USD 1 billion, of the total market in 2019. Out of this share, nanotechnology-based bone

[437] If the coating represents 2.5% of the stent's total cost (i.e. the same percentage as in the case of MRI-safe coated stents), the value of the coating materials will be USD 2.7 million.
[438] www.timplant.cz/en
[439] Durmus NG, Webster TJ (2012), Nanostructured titanium: the ideal material for improving orthopedic implant efficacy? Nanomedicine (2012) 7 (6): 791
[440] Mishnaevsky L Jr. et al. (2015), Nanostructured titanium-based materials for medical implants: Modelling and development. Materials Science and Engineering R 81 (2014) 1– Volume 81, July 2014: 2
[441] BCC Research (2014), Nanotechnology, a realistic market assessment
[442] BCC, ibid.
[443] Sahoo NG et al. (2013), Nanocomposites for Bone Tissue Regeneration, Nanomedicine. 2013; 8 (4): 639-653.
[444] BCC Research (2014), Nanotechnology, a realistic market assessment. p. 185
[445] http://cordis.europa.eu/result/rcn/82615_en.html

substitutes should capture at least half, or USD 500 million in sales, by 2019. Nanoparticulate bone substitutes such as Orthovita's VITOSS nanoparticulate bone filler, which has been on the market since 2000, have a substantial head start over nanocomposite-based products, which still must complete clinical testing before they are approved for use[446].

Case study: Bind Therapeutics

BIND Therapeutics is a clinical-stage nanomedicine platform company with the strong belief that Accurins™ represents the next stage in the evolution of targeted therapies and nanomedicine. Accurins™ is a new class of targeted and programmable therapeutics developed using a Medicinal Nanoengineering® platform. Accurins are nanoparticles designed with specified physical and chemical characteristics to target specific cells or tissues and concentrate a therapeutic payload at the site of disease, enhancing efficacy while minimising adverse effects on healthy tissues. The company is developing its own pipeline of Accurins, initially in oncology, as well as Accurins in collaboration with other biopharmaceutical companies like Pfizer, AstraZeneca etc.

BIND Therapeutics was founded in 2007 as Bind Biosciences, a commercialised entity emerging from MIT and Harvard. Bind Therapeutics has shown sustained amounts of investment in R&D by investing USD 13.1 million (EUR 9.8 million) in 2012, USD 24.4 million (EUR 18.3 million) in 2013 and USD 28.9 million (EUR 21.7 million) in 2014. Its recent revenue history has been as follows:

Revenues	2011	2012	2013	2014	2015
USD '000's	905	1047	10,901	10,426	9,000
EUR '000's	651	812	8196	7839	8,000

The company has 89 full-time employees, 70 of whom are primarily engaged in R&D activities.

BIND Therapeutics has collaborated or is collaborating with Pfizer, AstraZeneca, Roche, Merck, Macrophage Therapeutics (a subsidiary of Navidea Biopharmaceuticals, Inc.) and Amgen to develop Accurins based on therapeutic payloads and targeting ligands from their product pipelines. A snapshot of the relationships is as follows:

1. Pfizer: In March 2013, the company entered into a research, option and license agreement with Pfizer. The company granted to Pfizer two options to obtain an exclusive worldwide license to use, develop, manufacture and commercialise Accurins incorporating specified Pfizer small molecular targeted therapies (for the treatment, prevention and/or diagnosis of any disease or medical condition in humans). The licensed rights exclude some vaccine products and products for the treatment of brain cancer. Under the agreement, the company received an upfront payment of USD 4 million (EUR 3 million) in 2013 with the potential to receive contingent payments totalling up to USD 89.5 million (EUR 67 million) in the aggregate under each option upon exercise of the option and achievement by Pfizer of specified development and regulatory events, plus additional contingent payments totalling up to USD 110 million (EUR 83 million) in the aggregate under each option upon achievement by Pfizer of specified commercial events. The company achieved a development milestone in December 2014.

2. Merck: The Merck collaboration enables BIND to augment its own pipeline by accessing promising compounds from Merck's pipeline to use as payloads for Accurins. The first two compounds inhibit KSP and PLK1, important anti-mitotic targets that are key regulators of cell division and essential to the proliferation of cancer cells. Success in developing effective drugs that inhibit these targets has been limited by on-target but off-tissue toxicities, an ideal opportunity for development using Medicinal Nanoengineering platform. Under terms of the agreement, the company lead all aspects of product development prior to the end of Phase 1 and can choose to advance or terminate programmes at its sole discretion. At end of Phase 1, the company and Merck can choose to take products forward under a defined picking mechanism; the company will choose first, except in situations where Merck makes additional

[446] BCC assumes that nanocomposite bone replacement materials may be able to capture 10% of the total market for nanotechnology-based bone replacement materials, worth about USD 50 million, by 2019.

monetary or compound contributions to the collaboration.

3. Roche: The Roche collaboration is aimed at using novel approaches to target Accurins to tissues or compartments in the body that are difficult to access by conventional means. These targeting approaches may provide a pathway to create a pipeline of Accurins in therapeutic areas outside of oncology.

4. AstraZeneca: In April 2013, the company entered into a license agreement with AstraZeneca, pursuant to which the company granted to AstraZeneca a worldwide license to research, develop, manufacture and commercialise Accurins based on Barasertib (AZD1152), a potent selective inhibitor of the Aurora B kinase, for any therapeutic use in humans or animals. This license is exclusive with respect to BIND's intellectual property rights that arise under this agreement or the feasibility study that preceded it, and non-exclusive with respect to all of its IPR. Under the agreement, the company received an upfront payment of USD 4 million (EUR 3 million) in 2013 and have the potential to receive contingent payments totalling up to USD 193 million (EUR 145 million) in the aggregate upon achievement by AstraZeneca of specified clinical, regulatory and commercial events. The company will also receive tiered royalties in the low-single digit to the low-double digit percentages of aggregate worldwide net sales of licensed product, if any.

BIND owns more than 20 U.S. patents, has more than 40 pending U.S. patent applications that relate to medicinal nano-engineering platforms (as of December 2014). Of these licensed patents and patent applications, BIND licenses the majority on an exclusive basis, with the rest licensed non-exclusively to themselves. The company believes these patents and patent applications relate to advances in the nanoparticle field that are important for the development of a therapeutic nanoparticle. The issued patents generally are expected to expire by 2025 and 2030, and the applications that are pending, if issued to schedule, will expire by 2032 and 2035.

SUMMARY

The global market for products in nanomedicine (nano-pharmaceuticals and nano-diagnostics) is expected to grow from over USD 200 billion in 2013 to over USD 500 billion in 2019 (a compound annual growth rate (CAGR) of over 16%), with pharmaceuticals responsible for the larger share but diagnostics showing the larger growth rate (growing from 11% to 22% of the total and from USD 25 billion to USD 116 billion between 2013 and 2019). The global market for nano-pharmaceuticals is forecast to grow at a higher rate (CAGR 14.5%) than that for pharmaceuticals in general (CAGR 5.5%).

Of over 100 products identified here as being currently on sale, over half (56%) are nano-pharmaceuticals (i.e. drug delivery) and 13% are synthetic bone and tooth materials. One third of the products (31%) are aimed at cancer applications and almost one fifth (19%) counter infectious diseases. Products have been identified in areas including drug delivery (for cancer, cardiovascular, infectious disease and other applications); biomedical markers and detection (for cancer, cardiovascular and infectious disease applications); ferrofluids (for cancer and other applications); MRI contrast agents (for cancer applications); and surface disinfectants and antimicrobials (for infectious disease applications). Applications outside of the five sub-sectors include proteomics, synthetic bone, synthetic tooth enamel, transfection reagents, nano-porous membranes and drug production and mixing systems. In terms of the types of nanotechnology involved, two types (nano-porous membranes and antimicrobials) employ thin films or coatings; drug production and mixing uses nano-devices; and the rest use nanoparticles.

The largest markets and market forecasts are seen in materials (hydroxyapatite for synthetic bone and tooth enamel, USD 1.1 billion in 2019) and for drug delivery (USD 214 million by 2019) and potentially in new areas such as quantum dots (USD 435 million in 2019 for biological reagents using quantum dots) and proteomics, albeit that these are areas of great uncertainty in terms of how research will progress, whether approvals will be given and to what extent the cost will be a factor. For proteomics, the market for conventional arrays is forecast to grow to USD 8.2 billion in 2019 but it is hard to predict what share of the market nanotechnology will capture.

The economic downturn is leading governments to try to reduce healthcare costs and many of the treatments that incorporate nanotechnology have premium pricing. Reimbursement of such high-cost drugs is becoming a hurdle for the growth of such markets. Some areas in which nanotechnology has been applied successfully (e.g. MRI contrast reagents using iron oxide nanoparticles) have suffered a drop in demand related to the high cost of their use and the arrival of alternatives (some

of which are also nanotechnology-based (e.g. gadolinium reagents) but which have not yet fully gained market share).

The next section looks at the wider environment for health nanotechnology – regulation and standards, environmental health and safety issues, communication and public attitudes.

11 THE WIDER ENVIRONMENT FOR NANOTECHNOLOGY AND HEALTH

11.1 Regulation and standards for nanotechnology

11.1.1 European regulations for nanotechnology

In terms of nanotechnology regulation, the European Union is well-advanced but not alone in seeing the need for greater scrutiny on the use of nanotechnologies for medical purposes. To facilitate regulation, inter alia, a definition of nanomaterials has been defined by the European Commission in its Recommendation on the Definition of a Nanomaterial - 2011/696/EU. This non-binding document has also been used by other pieces of regulation to define the term 'nanomaterial'.

The table below lists some key regulatory documents within the European Union and within its Member States. Nano-specific regulations often exclude medicinal products and medical devices from their scope due to the specific rules applying to the medical industry. These regulations are nevertheless relevant to the health sector as they may come into force at different stages of the production process (e.g. at the manufacturing stage of a batch of nanomaterials with uses in various sectors).

Table 11-1: Overview of regulations for nanotechnology use in Europe

Status	Name of the document	Country /Region	Scope	Nano-specific
Implemented	Regulation concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) - 1907/2006(EC)	EU	Chemicals & Raw Materials, excludes medicinal products and substances in medical devices from some requirements.	No, but 'substance' covers nanomaterials
Under review	Regulation on Medical Devices - 2012/0266(COD)	EU	Medical devices	Yes
Implemented	European Commission Recommendation on the Definition of a Nanomaterial	EU	Substances at the nanoscale (including medicinal products)	Yes
Implemented	Nanomaterials in the Healthcare Sector: Occupational Risks & Prevention - E-fact 73	EU	Medical devices and pharmaceuticals (and wider healthcare)	Yes
Implemented	Decree on the annual declaration on substances at nano-scale - 2012-232	France	Substances at the nano-scale (including medicinal products)	Yes
Published	Guidance on the Determination of Potential Health Effects of Nanomaterials Used in Medical Device	EU	Medical devices	Yes
Implemented	Royal Decree regarding the Placement on the Market of Substances manufactured at the Nano-scale	Belgium	Substances manufactured at the nano-scale (excluding those in medicinal products/ medical devices)	Yes
Implemented	Order on a Register of Mixtures and Articles that contain Nanomaterials as well as the Requirement for Manufacturers and Importers to report to the Register – BEK no. 644	Denmark	Nanomaterials (excluding those used in medicinal products and medical devices)	Yes

There are also efforts underway within the research community to develop a testing strategy for engineered nanomaterials such as those used in some health and cancer treatment applications. These include the ITS-NANO project under FP7-NMP which seeks to establish a roadmap for the development of advanced tools and databases that help to assess the risks through knowledge-based decision making.[447]

11.1.2 Nanotechnology regulation in the rest of the world

A 2013 publication of the OECD on the *Regulatory Frameworks for Nanotechnology in Foods and Medical Products*[448] disclosed the results of a survey on 10 OECD delegations from the EU, France, Germany, the Netherlands, Poland, Canada, Japan, Norway, the Russian Federation and the USA. According to this survey, all the aforementioned delegations have frameworks 'governing the manufacture, importation and commercialisation/marketing for medical products relevant to nanotechnology'. All of them also stated that they had 'published (or articulated) a regulatory approach to nanotechnology'; these approaches are not systematically reported in the document. The OECD concluded that, in the countries of the responding delegations, the existing frameworks already cover medical products that may contain nanomaterials or involve the application of nanotechnology.

11.1.3 Standardisation and nanotechnology

Nanotechnologies in the field of medicine have also been considered by standardisation bodies. At European level, the European Standardisation Committee (CEN) has a dedicated technical committee TC 352 that has been working with nanotechnologies. While the organisation's working group WG3 is focussing on 'Health, Safety and environmental aspects', it has not yet published any document directly relating to nanomedicine.

At the international level, the International Organisation for Standardisation (ISO) is responsible for the standardisation of nanotechnologies with its TC 229. Similar to CEN/TC 352, the International Technical Committee comprises a working group on health safety and environmental aspects.

The seventh part of the ISO 80004 series on nanotechnology vocabulary is dedicated to nanomedicine (ISO/TS 80004-7:2011 Nanotechnologies - Vocabulary - Part 7: Diagnostics and therapeutics for healthcare). It defines general terms such as 'nanointervention' (i.e. manipulation at the cellular and subcellular level using nano-scale properties of materials or systems), as well as terms related to structural entities (e.g. 'stealth nano-object', 'nanoarray', 'nanopore sensor', 'nanocapsule', etc.).

While standardisation bodies have nanotechnology committees, nanotechnologies are cross-sectoral and are therefore relevant in other specific TCs of ISO. The EU FP7 project NanoSTAIR identified all ISO/TCs working with nanotechnologies. At the international level, the consortium identified several relevant technical committees working with health issues:

- ISO/TC 150 Implants for surgery;
- ISO/TC 150/SC2 Cardiovascular implants and extracorporeal systems;
- ISO/TC 194 Biological evaluation of medical devices; and
- ISO/TC 215 Health informatics.

ISO/TC 194 is also currently developing a specific guidance on nanomaterials for the biological evaluation of medical devices (ISO/NP TR 10993-22); this document is still in draft stage.

11.2 Health regulations and nanotechnology

In order to protect the consumer, the health sector is highly regulated. There are three major health application areas each having different regulatory requirements attached to them: medicinal products, medical devices and advanced therapy medical products. Testing of the products is required and can greatly increase the cost and time to market of new or changed products. The process of testing, leading to a market authorisation, takes the form of a benefit and risk analysis which

[447] http://www.its-nano.eu

[448] OECD (2013), "Regulatory Frameworks for Nanotechnology in Foods and Medical Products: Summary Results of a Survey Activity", OECD Science, Technology and Industry Policy Papers, No. 4, OECD Publishing. http://dx.doi.org/10.1787/5k47w4vsb4s4-en

examines the three elements of quality, safety and efficacy of the medicine or medical device.

Following the acquisition of the market authorisation, the pricing of the product has to be negotiated and the terms for reimbursement set. These negotiations involve regional, national and private health insurance authorities.

In the EU, the framework under which these health products are brought to the market is based on the following EU Directives and Regulations, amongst others:

Table 11-2: European directives and regulations for health products

Application	Directives and Regulations
Drugs Including Nano-Pharmaceuticals	Directive 2001/83/EC on Medicinal Products for Human Use Regulation No.141/2000 EC for new therapies for orphan diseases ('orphan drugs').
Medical Devices[449]	Directive 93/42/EC on Medical Devices Directive 98/79/EC on in vitro diagnostic medical devices
Advanced Therapy Medical Products	Advanced Therapy Medical Products (cell therapies and regenerative medicine). Regulation EC No 1394/2007 for gene and cell therapies.
Clinical Trials	Clinical Trials Regulation (CTR) EU No 536/2014
Good Clinical Practice	The Good Clinical Practice Directive 2005/28/EC
Good Manufacturing Practice	Directive 2003/94/EC
Animal Testing (in vivo, pre-clinical testing)	European Directive 2010/63/EU ("Directive") on the protection of animals used for scientific purposes

In addition to different regulations and directives, the bodies responsible for accrediting new health products vary from one type to another.

- New pharmaceutical products require an application to be made to the EMA (European Medical Association), working in cooperation with national agencies, and the products follow a centralised procedure at the EU level.
- Approval of medical devices (including bandages, implants, medical instruments and equipment) must be obtained from authorised national 'Notified Bodies', which give the product a CE marking. There are four classes of medical devices depending on their intended purpose and inherent risks. Following the reporting of the supply of breast implants filled with sub-standard silicone by PIP, the EC proposed in September 2012 a new Regulation on Medical Devices, and the amendment of the previous Directive and regulations. This proposal is in discussion in the European Council and Parliament.
- The regulatory framework for advanced therapy medical products is under responsibility of EMA.

REGULATION IN OTHER PARTS OF THE WORLD

European products are also subject to regulatory frameworks in other countries if they are to be marketed abroad. Marketing authorisations have to be applied for in each region or country and there are considerable differences between, for example, the US (implemented by the FDA[450]), Canada, Australia, China and Japan. A product approved for the EU countries generally must be clinically tested again to gain approval in the US, incurring additional costs and time delays.

In order to harmonise regulation globally, the International Conference on Harmonisation of Technical

[449] See also http://ec.europa.eu/growth/sectors/medical-devices/regulatory-framework/revision/index_en.htm
[450] US Food and Drug Administration http://www.fda.gov/

Requirements for Registration of Pharmaceuticals for Human Use (ICH)[451] convenes meetings of the regulatory authorities[452] and pharmaceutical industry to discuss scientific and technical aspects of drug registration. Members currently come from Europe, Japan, USA, Canada and Switzerland but expansion is being considered. ICH meetings aim to share regulatory understanding and activities, learn from existing regulatory frameworks and policy approaches, and promote regulatory convergence where appropriate. Confidentiality agreements are used to enable more open sharing of information among regulators.

11.3 Environment, health and safety and nanotechnology

In the health-related nanotechnology, the drivers for innovation and market development are mainly linked to the possible economic and therapeutic impact and the perceived societal needs that may be met by the application of this new technology in pharmaceuticals and medical devices. Some nanotechnologies appear useful in reducing the effect on the environment of what previously were considered to be undesirable chemicals.

A constraint to the development of nanomedicine is the lack of sufficient and suitable data to estimate the environmental and the health risks associated with nanomedicine products. This is particularly the case for the human health risks, since from the inventory made in a pilot report on "EHS issues of selected nanomaterial values chains and their market prospects", it appears that environmental risks are probably low. A key mitigating factor is that, even if nanomaterials were to be widely used in medical applications, the total tonnage of materials used will be small.

11.4 Communication, public attitudes and societal issues

11.4.1 Printed and online media

A search on the web and in news media of terms related to nanotechnology and health[453] shows (see table below) that diabetes is the sub-sector with most articles on the web and infectious disease has the most news items relative to general websites, the latter probably due to the recent Ebola crisis. While these data are approximate, they may be useful in identifying where the public can find the most information, relatively speaking, on a given nanotechnology and health topic. The number of news items is an indication of where the media perceive that the interest of the public lies.

Table 11-3: Frequency of articles on the web, in the news for nanotechnology health topics

Keyword Category	Web, Thousands	News, Thousands	News / Web, %
Cancer Treatment	398	4.0	1.0
Cardiovascular Disease	344	1.3	0.4
Diabetes	1280	15	1.1
Infectious Diseases	267	3.6	1.3
Neurodegenerative Disease	79	0.09	0.1

A second search was done in order to obtain an indication of where the interests of academics lie. Using Google Scholar[454], it was found that cancer treatment and diabetes are the primary focus of academics working on the five health sub-sectors.

[451] http://www.ich.org/home.html

[452] Participating organisations include the European Medicines Agency, European Commission, European Food Safety Authority, Health Canada, Japanese Ministry of Health, Labour and Welfare and Pharmaceuticals and Medical Devices Agency, United States Food and Drug Administration.

[453] The search was carried out using the keywords in quotation marks, coupled with the term nano*, so all words beginning with nano are included.

[454] Google Scholar is an online database of many of the peer-reviewed online journals of Europe and the US, plus books and non-peer reviewed journals, containing an estimated 160 million documents in 2014 (Orduña-Malea, E, *et al.* (2014). About the size of Google Scholar: playing the numbers. Granada: EC3 Working Papers, 18: 23 July 2014.)

Table 11-4: Frequency on Google Scholar of nanotechnology health topics

Keyword Category	Scholar, Thousands	Scholar/Web %
Cancer Treatment	70	10
Cardiovascular Disease	33	10
Diabetes	91	7
Infectious Diseases	17	6
Neurodegenerative Disease	8	10

Of the top 100 new items on nanotechnology in cancer treatment (search term: "cancer treatment" nano*), nearly 40% are from general interest websites aimed at the general public, much greater than in the other nanotechnology sectors, as shown in the figure below. As well as scientific and technologically-focused news articles, 10% were business-related and featured private companies using nanotechnology to treat cancer.

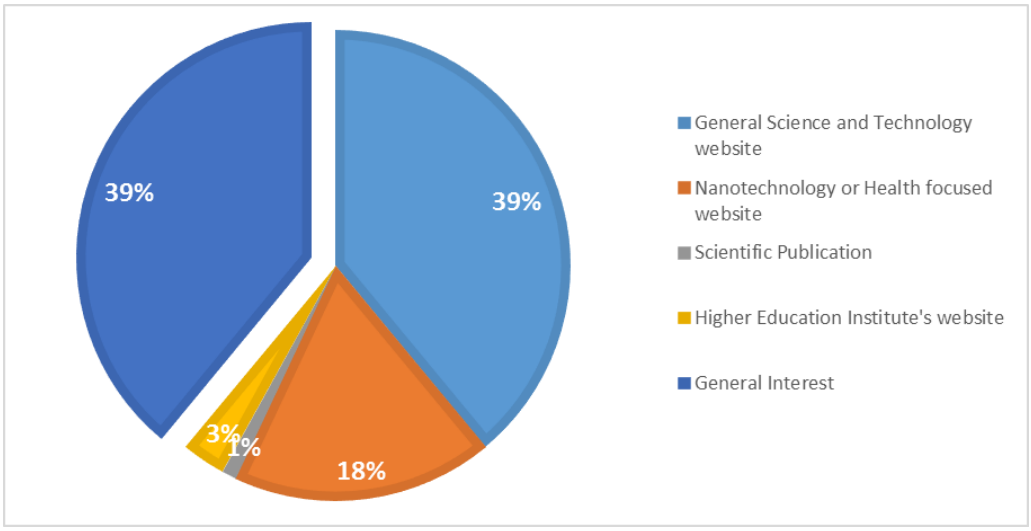


Figure 11-1: Type of website for the top 100 news items for nanotechnology and cancer treatment

Research into nanotechnology in the five health sub-sectors has increased over the last decade, as shown in the figure below. Reports of how nanotechnology can provide non-invasive diabetes monitoring are more numerous than those concerning the treatment and diagnosis of the medical conditions in the other sub-categories. This maybe because glucose-sensing is something of a low-hanging fruit for nanotechnology. Getting nanotechnology to work outside the body is much simpler than delivering, targeting or using nanotechnology inside the body as is necessary with the medical conditions excluding diabetes. Nevertheless, research in all the sub-sectors of nanotechnology in health is growing, indicating there are still many outstanding challenges within each area.

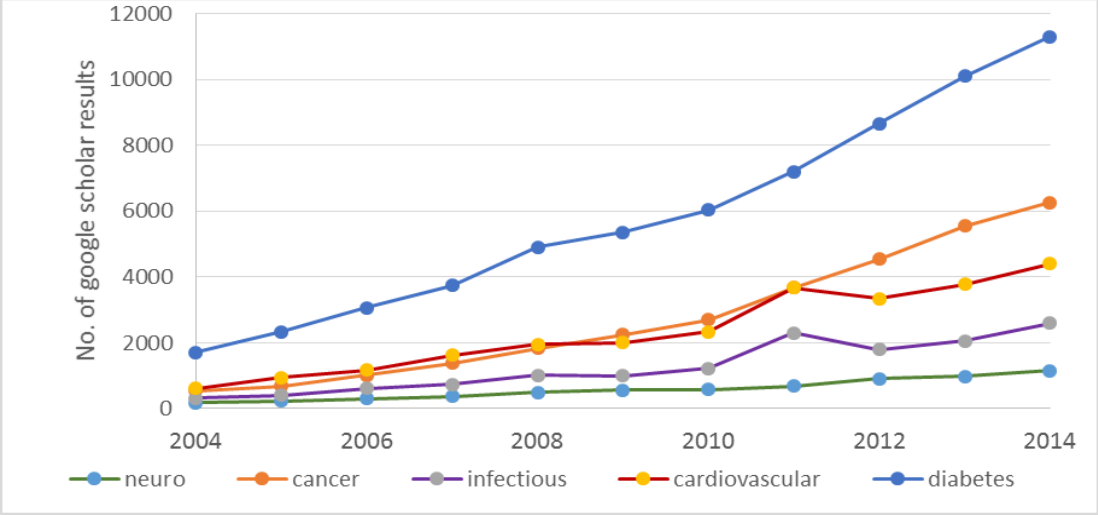


Figure 11-2: Trends over time in Google Scholar results for the health nanotechnology sub-sectors

More than 200 scientific journals regularly publish articles on nanotechnology[455]. For the academic community, the International Scientific Journal & Country Ranking (SJR) index provides a means of identifying which are perceived to be the most prestigious. The h-5 index is a measure of the number of highly cited articles, and is thus dependent on how many articles are published annually by the journal. The top five journals, as measured by the SJR index largely follows the metric of citations per document published, as shown in the table below.

Table 11-5: Bibliometric data for nanotechnology

Title of journal	SJR	h-5 index 2010-14	Total articles (3 years)	Citations per article (2 years)	Country
Nature Nanotechnology	17.0	140	626	23.8	UK
Nano Letters	9.4	181	2940	13.2	US
Advanced Materials	7.9	190	2511	15.2	DE
Nano Today	7.8	61	195	17.4	NL
ACS Nano	7.0	170	3387	12.0	US

Source: http://www.scimagojr.com/journalrank.php?category=2509

While it should be noted that many nanotechnology publications may not have a Facebook page, one indication of popularity of nanotechnology media can be seen in the figures for the number of "Likes" on Facebook:

Table 11-6: Facebook likes as a measure of interest in nanotechnology

Facebook Page	Likes
Nanotechnology	99,000
Nanotechnology World Association	33,000
Nanotechnology Now	6,400
Nanotechnology Solutions	3,500
Nanowerk Media/News/Publishing	5,400
The International Nano Science Community	5,700
Nanobiotechnology	2,100

[455] http://www.nanowerk.com/nanotechnology/nanotechnology_periodicals.php

This information may be useful in targeting any information for the public in future over and above the EC's own web pages.

11.4.2 Surveys of the public

More rigorous measures of public awareness, attitudes and communication can be seen through surveys but public surveys on nanomedicine have been scarce so far. Although not representative for the 'average' EU-citizen, the results provide some indications of trends in attitudes.

NanOpinion was an FP7 project, which ran from 2012 to 2014, focused on monitoring public opinion on nanotechnology in Europe[456]. An online hub, social media, education and information booths in public spaces and special events were used to develop a dialogue with the general public about nanotechnology. Over 1,500 questionnaires were completed in which participants answered questions designed to gauge their understanding and opinions of nanotechnology.

Analysis of the questionnaires revealed that Europeans in general have little understanding of nanotechnology but are generally interested in and positive about it. Respondents expected information on nanotechnology to be honest and balanced and wished there was more information available, particularly in the popular media. Across all educational backgrounds, they would be interested in buying products, including food containers, clothing and sun cream, containing nanomaterials. However, they would like to see nano-containing products labelled with detailed information and the testing and regulation of these products carried out by independent national or international bodies rather than profit-oriented companies. Their main policy recommendations were to promote consistent and detailed product labelling carried out by an independent body, to update teachers' knowledge of nanotechnology and to encourage more interdisciplinary STEM (science, technology, engineering and mathematics) curricula.

The objectives of NanoDiode, an FP7 project running from mid-2013 to mid-2016, is to develop a co-ordinated and innovative strategy to engage EU civil society in a dialogue about responsibility around nanotechnologies[457]. As part of their approach they reviewed the experiences and outputs of previous European projects on nanotechnology dialogue and outreach in order to identify best practices they could adopt for educational workshops and other activities[458]. The scope of NanoDiode is more ambitious than NanOpinion in as much as they aim to facilitate dialogue across all levels of the nanotechnology value chain, from the general public to policy makers. Through outreach, education and specific events they will involve a cross-section of researchers, industrialists, citizens, scientific advisers and policy makers with the aim of learning where and how society wish nanotechnologies to be applied. For example, they aim to bring groups of potential nanotechnology 'users' (industrial customers as well as consumers) together with researchers working on near-market products in order to facilitate discussions which could help steer the research towards social values and user needs.

In addition to these FP7 projects, two population surveys in Germany provide some data on the public's attitudes, with a few results relevant for nanomedicine (Zimmer et al, 2009)[459], as well as a survey among young people conducted within the framework of the NANOYOU project (NANOYOU, 2010)[460] and a recent survey in the USA (Shipman, 2010)[461]. Work has also been undertaken by the OECD on public engagement with nanotechnology and a guide produced to assist policymakers in working with the public on issues related to nanotechnology (OECD, 2010)[462].

Relatively favourable situations may exist if citizens have concrete experiences with, or expectations towards specific applications; they tend to support applications "that are linked to a wider social good

[456] www.nanopinion.eu
[457] www.nanodiode.eu
[458] Analysing previous experiences and European projects on nanotechnology outreach and dialogue and identifying best practices, Daan Schuurbiers and De Proeffabriek, March 2014, (Accessed at http://www.proeffabriek.nl/uploads/media/NanoDiode_WP1_Best_Practices.pdf in November 2015)
[459] Zimmer, R., Hertel, R., Böl, G.F., 2009, "Public perceptions about nanotechnology: Representative survey and basic morphological-psychological study", Bundesinstitut für Risikobewertung (BfR)
[460] Nanoyou, 2010 http://cordis.europa.eu/publication/rcn/15319_fr.html
[461] Shipman, M., 2010, "Hiding risks can hurt public support for nanotechnology", News Services of the North Carolina State University
[462] http://www.oecd.org/sti/biotech/49961768.pdf

or perceived individual benefit" (Böl, 2010; Fleischer et al., 2012)[463,464]. This may very well be the case for medical and especially for cancer therapy applications.

Table 11-7: Assessments by the public of various applications of nanotechnology
From German online discourses and a questionnaire survey (Böl et al. 2010)

Application	Ratio of Positive to Negative Assessments	
	Online Discourses	Population Survey
Cancer Therapies	90 : 10	(not asked)
"Other Serious Medical Applications"	88 : 12	87 : 13
Surface Treatment (textile & vehicle)	67 : 33	93 : 7 (paints) 91 : 9 (textile)
Cosmetics (excl. sunscreens)	59 : 41	51 : 49
Textile; other than Surface Treatment	56 : 44	76 : 24
Food Packaging	25 : 75	81 : 19 (detection) 64 : 36 (foil quality)
Foodstuffs	10 : 90	25 : 75 (lump prevention) 10 : 90 (appearance)
Sunscreen Products	10 : 90	78 : 22
Dietary Supplements	0 : 100	not asked

In approximately 50% of the postings relating to medical applications, mainly benefits were expected, while in only 5% of the postings mainly "harm" was expected (Böl, 2010). In the most recent years analysed - 2007 and 2008 - an increase in the fraction of positive assessments of medical applications was seen.

In another recent survey in the USA, 849 respondents were included, and it appeared that "support for therapeutic applications of nanotechnology was strong, while support for human enhancement applications much less" (Shipman, 2010).

11.4.3 Societal issues

An evaluation of a number of qualitative, country-specific studies in the Eurobarometer pointed out that if the public expects benefits of nanotechnologies, medical applications in particular are mentioned (Eurobarometer, 2010)[465]. The specific benefits expected include improved disease prevention, early disease detection and improved medical treatment. On the other hand, in addition to general concerns about the lack of knowledge on the (health) risks of nanomaterials, European citizens felt that in the case of medical applications, "the collection of increasingly sensitive data in medical diagnosis and its distribution", potentially enabled by nanotechnologies, were reasons for concern.

Societal issues and concerns, including stakeholder positions, have been more thoroughly dealt with in a few 'landmark' initiatives, including the NANOMED and the European Group on Ethics

[463] Böl, G.F., Epp A., Hertel, R., 2010, "Perception of nanotechnology in internet-based discussions", Bundesinstitut für Risikobewertung (BfR)
[464] Fleischer, T., Jahnel J., Seitz S.B., 2012, "NanoSafety – Risk governance of manufactured nanoparticles", European Commission
[465] Eurobarometer 2010, special issue 314 report

Roundtables[466,467], ObservatoryNano initiatives[468,469], a joint JRC/IPTS-report[470], the European Commission's public consultation on the Strategic Nanotechnology Action Plan 2010-2015 (EC 2010), and stakeholder position documents[471] from the EEB, ETUC and BEUC.

The 716 stakeholders responding to the European Commission's public consultation on the SNAP 2010-2015 universally regarded applications in healthcare as 'very promising', although the perception of possible risks was clearly present as well (see table below) (EC 2010[472]).

Table 11-8: Perception of benefits and risks of nanomedicine
As observed by respondents to the EC's public consultation on SNAP 2010-2015 (n = 716) (EC 2010)

	Very High	High	Modest	None
Benefits	50%	32%	10%	3%
Risks	16%	29%	35%	11%

Various scientists and stakeholders, including patients' organisations, have warned against 'overselling' nanomedicine, and against creating unrealistic expectations. To this end, in the Roundtable on the Ethical Aspects of Nanomedicine organised by the European Group on Ethics it was stated "headline journalism has not helped to distinguish science-fiction from science-fact"[473]. The participants in the NANOMED Roundtable very clearly defined the potential threat that "the 'nanomedical community' might not be able to fulfil the expectations of a hopeful public before it becomes disillusioned" (Nanomed, 2010).

Many technological developments in nanotechnology are only predicted to date and have not yet materialised (Gammel 2009)[474]. There have been some strong predictions that are yet to come to fruition and seem unlikely to do so in the associated timeframe (e.g. by the USA cancer programme, which in 2004 claimed that cancer suffering and death would end by 2015 (Gammel 2009)). At the same time, some literature notes that nanotechnology has been applied in few treatments so far (Nanodiara, 2011)[475]; although in the NANOMED Roundtable it was observed that 45 different types of nanomedicine products had already entered the market (Nanomed, 2010).

Unrealistic claims and promises may easily lead to disappointment and loss of trust of the public, and thus, to a lack of support and acceptance of future nanomedicine applications. The claims of benefits of novel nanomedicine applications should at least be plausible, and preferably proven. Indeed, one conclusion from an analysis of online discourses on nanoproducts was that the doubts about the benefits could do more harm to the acceptance of future nanoproducts than fears about 'unconfirmed' risk (Böl, 2010). At the same time, a high level of general mistrust in industry was observed in this analysis. However, this result may be biased by the specific subgroup of consumers, which consisted of active online responders.

In nanomedicine, a major issue is the fact that innovative diagnoses will probably develop much faster than therapies (Gammel, 2009). This may "leave more and more people confronted with devastating diagnoses but without hope", and with "data you never asked for, didn't want to know, and which might be misused or lead to genetic discrimination" (Gammel, 2009). A 'right not to know'

[466] Nanomedicine ethical, regulatory, social and economic environment (NANOMED), 2011, "Nanomed Round Table Report"
[467] European Group on Ethics in Science and New Technologies to the European Commission (EGE), 2006, "The ethical aspects of nanomedicine; Roundtable report"; European Group on Ethics in Science and New Technologies to the European Commission (EGE), 2007, "Opinion on the ethical aspects of nanomedicine"
[468] Malsch, I., 2012, "Communicating Nanoethics: Annual report 4 on Ethical and Societal Aspects", ObservatoryNano
[469] ObservatoryNano, 2011, "Health & Medicine sector evaluation"
[470] Wagner, V., Hüsing, B., Gaisser, S., Bock, A.K., 2008, "Nanomedicine: Drivers for development and possible impacts", Joint Research Centre
[471] For example, Joint environmental and consumers' NGOs, 2012, "Stakeholders' Response to the Communication on the Second Regulatory Review on Nanomaterials"
[472] The European Commission's public consultation on the Strategic Nanotechnology Action Plan 2010-1015
[473] European Group on Ethics in Science and New Technologies to the European Commission (EGE), 2006, (see previous reference)
[474] Gammel, S., 2009, "NanoEthics portfolio", NANOCAP-project - available at: www.nanocap.eu (date last accessed: 4 November 2013)
[475] http://www.nanodiara.eu/news-archive/

was highlighted in the NANOMED Roundtable discussions as well (Nanomed, 2010). The participants added that new nano-diagnostic capabilities may empower citizens, but may also exploit their vulnerabilities and anxieties. Safeguards should be provided in public healthcare systems, and medical professionals and manufacturers should take their responsibility (Nanomed, 2010). The discussions are taking place in relation to nanotechnology-based applications, albeit that the topic is a general one for the medical field, and there may be few issues which are specific only to health-related nanotechnology and nanotechnology for cancer.

12 CONCLUDING SUMMARY

Health nanotechnology is being supported through measures at national and European levels to enable researchers to produce publications and engage in projects that increase knowledge that is being patented and commercialised into products.

Throughout Framework Programme projects, publications and patents, it is seen that researchers, organisations and companies from a small number of countries prevail. For the EU28, actors in Germany, the UK and France lead the way, followed by those in Spain and Italy. (The Netherlands also performs strongly in projects, less so in publications and patents.) This reflects in part the size of the countries, the size and strength of their research bases and their ability to fund research and development at a large scale. Certain organisations, again large and well-resourced, also lead in project and patent outputs – CNRS (France) and CSIC (Spain), as well as the Swiss institution ETHZ, for example.

Companies are not so engaged in European projects - with a small number of notable exceptions such as Philips - or in publications, these being dominated by higher education institutions.

Looking at the trend in numbers, 200,000 publications on health nanotechnology have been found over a fifteen-year period, an average of over 13,000 per annum. In a similar period, approximately 200 patents were filed at the European Patent Office. The search for products has revealed over 100 health nanotechnology products on the market.

Nanotechnology is mainly being used in products in the fight against cancer and this is also the area in which the most publications and projects occur, the most European funding is spent and the most patents are filed.

Over ninety companies were found to produce products for health using nanotechnology. While some big names were represented (e.g. Abbott, Bayer, Merck, Pfizer, Novartis and Smith & Nephew), there was also a high representation of SMEs.

Health nanotechnology has been estimated to employ over 100,000 people in Europe and to create added value of over EUR 16 billion. With compound annual growth rates for products of 10% and more, it is expected that these figures will continue to increase over the coming decades.

ANNEXES

ANNEX 1: METHODOLOGIES FOR LANDSCAPE COMPILATION REPORTS

The outline of this report is as follows:

- Introduction;
- Development of keywords;
- Methodology by task and sector: projects, publications, patents and products;
- Methodology for additional information: markets, wider economic data, environmental health and safety, regulation and standards; and
- Concluding remarks.

A Introduction

This paper outlines the main methodologies used in the NanoData project.

The data were in large part identified using keywords to search existing databases (e.g. for publications and patents) and to select projects (from eCorda) and products (e.g. from product databases). The report explains how the keywords were identified and what quality control measures were put in place.

It should be noted that eight sectors were included in the work – construction, energy, environment health, ICT, photonics, manufacturing and transport. Thus, the data are not comprehensive across all of nanotechnology. They are, instead, representative of the sectors selected within the context of the overall project for the European Commission.

B Development of keywords

The keywords were identified from known data sources, web searches and expert input. They were validated through discussions with consortium members[476] (where they had expertise and experience in the area concerned) and other experts. Following that validation process, the keywords were also tested by one or both of the following methods:

- The word 'nano' and the keywords were used to select the FP projects relevant to the sector (and sub-sectors if appropriate). The projects identified were checked manually for false positives. False negatives were also identified (projects that were expected to be selected that were not). The keywords were refined to optimise the number of projects correctly selected.
- The keywords were used to select publications. The lists of publications were checked, in part manually and in part semi-automatically using the CWTS VOSViewer bibliometric mapping tool (http://www.vosviewer.com/Home). Using the tool, it was possible to see how terms group together in publication space (by their proximity on a VOSViewer map) and how often they occur (by their size on the VOSViewer map). Thus, it was possible to determine which terms would be the most significant in the sector and also which terms would be likely to cause false positives. For example, in the partial map for nanotechnology and health below (bottom left corner) it can be seen that a very important term is 'scaffold', and related terms are about tissue and bone engineering. Moving further to the right, the related term 'biocompatibility' is seen and nearby the significant and related but more generic terms 'surface', 'morphology' and 'synthesis'.

[476] Partners of the Joint Institute for Innovation Policy for this project i.e. CWTS, Frost & Sullivan, Joanneum Research, Oakdene Hollins, the Nanotechnology Industries Association, Tecnalia and TNO.

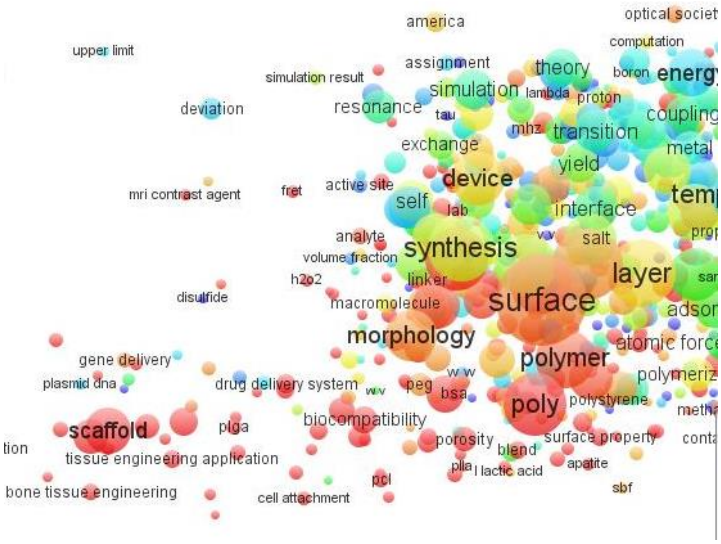


Figure A: Partial VOSViewer map for nanotechnology and health

Additional terms could also be identified for inclusion in the keyword list.

It should be noted that, where the use of a keyword could lead to false results, the keyword was omitted. This inevitably leads to some data of relevance being omitted from the resource base of the project, the alternative being the inclusion of much irrelevant information. For example, some words (e.g. photodetector, laser, photolithography) were omitted from the keywords for photonics as they have much wider applications that photonics alone.

In the searches, keywords were truncated to maximise the possible results. For example, in energy, "thermoelectric*" could identify data related to "thermoelectric", "thermoelectrics", "thermoelectrical" and "thermoelectricity", the * indicating the truncation.

Where possible, both British and American spellings were included (e.g. tumour and tumor) as were alternative spellings (e.g. orthopaedic and orthopedic).

Methodology by task and sector

C Framework Programme projects

The Framework Programme (FP) project details were provided by the European Commission from the eCorda database for FP6 and FP7. Abstracts for the FP6 projects were provided separately as these were not in the original database received. The total number of FP projects in eCorda database is 35,365 of which 25,238 are FP7 projects and 10,027 FP6 projects. These projects involved 210,177 participations by researchers of which 76,562 are in FP6 and 133,615 in FP7.

The table below presents an overview of the data for FP6 and FP7 according to the variables used in the NanoData analysis. It also identified the number of missing values per variable. It shows that the eCorda database is a nearly complete source of FP6 and FP7 project data and participant data with only relatively few data missing (between 2.4% and 0% of the total for FP6 and FP7 depending on the variable).

Table A: Number of actual observations and missing values for each of the eCorda variables used for the NanoData analysis.

Variable	Number of observations						
	FP6		FP7		Total		
	Actual	Missing	Actual	Missing	Actual	Missing	% Missing
Project ID	10,027	0	25,238	0	35,265	0	0.0%
Start date	9,966	61	24,906	332	34,872	393	1.1%
End date	9,965	62	24,906	332	34,871	394	1.1%
Duration	10,027	0	25,238	0	35,265	0	0.0%
Number of partners	10,027	0	25,238	0	35,265	0	0.0%
Specific Programme	10,027	0	25,238	0	35,265	0	0.0%
Sub-Programme[477]	10,027	0	25,238	0	35,265	0	0.0%
Call	9,989	38	25,238	0	35,227	38	0.1%
Instrument	1,0027	0	25,238	0	35,265	0	0.0%
EC contribution	10,027	0	25,238	0	35,265	0	0.0%
Project total cost	9,771	256	25,238	0	35,009	256	0.7%
Project ID	76,562	0	133,615	0	210,177	0	0.0%
Participant ID	76,550	12	133,615	0	210,165	12	0.0%
Participant role	76,562	0	133,615	0	210,177	0	0.0%
Participant legal name	76,561	1	133,615	0	210,176	1	0.0%
Participant country[478]	76,562	0	133,615	0	210,177	0	0.0%
Participant region	76,562	0	133,615	0	210,177	0	0.0%
Participant organisation type	74,271	2,291	133,615	0	207,886	2,291	1.1%
EC contribution per participant	71,748	4,814	133,569	46	205,317	4,860	2.4%
Project cost per participant	72,960	3,602	133,575	40	206,535	3,642	1.8%

In the eCorda database, the EC contribution per project shows some small differences between the data presented by project (project database) and the data presented by participant (participant database). The table below illustrates the differences, both in millions of euros and as shares of the EC contribution. It can be seen that the difference in EC contribution between the project and participant data is almost zero in FP7 and small in FP6. However, the differences can become significant when the data is aggregated.

[477] In FP6 these were called Priorities and in FP7 Work Programmes.
[478] The report uses ISO 2-digit codes for countries. See http://www.iso.org/iso/country_codes

Table B: Number of projects and EC contribution for the project data and participant data in eCorda

	Number of projects		EC contribution (MEUR)		Difference (Project – Participant) (MEUR)	Difference %
	Project Data	Participant Data	Project Data	Participant Data		
FP						
FP6	10,027	10,027	16,692.320	16,653.860	38.460	0.23%
FP7	25,238	25,238	44,917.330	44,917.200	0.130	0.00%
Total	35,265	35,265	61,609.650	61,571.060	38.600	0.06%
NT						
NT-FP6	908	908	1,702.740	1,695.500	7.250	0.43%
NT-FP7	2,636	2,636	4,660.840	4,660.750	0.090	0.00%
Total	3,544	3,544	6,363.580	6,356.250	7.340	0.12%

C1 Classification of projects

C1.1 Classification of nanotechnology projects

In order to identify the baseline set of nanotechnology-related projects for the NanoData work, a search was made for all FP projects that contained 'nano'[479] in the title or abstract of the project. 3,544 projects were selected in this way[480], of which 74% were FP7 projects and 26% were FP6 projects. Comparing the distribution of projects between FP6 and FP7 for nanotechnology and for the two FPs overall, it is found that the distributions are very similar the latter being 72% in FP7 and 28% in FP6. Nanotechnology projects make up 10% of Framework Programme projects, the share increasing slightly from FP6 (9.1%) to FP7 (10.4%).

The table below shows the distribution of total FP projects and of nanotechnology projects.

[479] The term "nano" could appear as a part of a word (e.g. nanotechnology, nanoscience, nanomaterial, nanoscale), as a part of compound word separated with hyphen (e.g. nano-science) or as an independent word "nano".

[480] Unlike the other sectors considered by the project (HT, EN, PH, MF), for ICT additional projects were identified by use of keywords such as graphene. These were judged to be too important in ICT to be omitted. This did, however, result in the total number of nanotechnology projects being different for ICT (4,143) and the other sectors (3,544).

Table C: Number and share of nanotechnology projects in FP6 and FP7

		Total	FP7	FP6
FP total	Number of FP projects	35,265	25,238	10,027
	Share of FP (total)	100%	71.6%	28.4%
Nanotechnology	Number of FP projects	3,544	2,636	908
	Share of FP	100%	74.4%	25.6%
Share of nanotechnology of total FP		10.0%	10.4%	9.1%

C1.2 Classification of projects by sector and sub-sector

The 3,544 projects relevant to nanotechnology were subjected to a search using the sector keywords to identify projects relevant to each sector. This search was undertaken using the keywords identified for each sector. The project details for the selected projects were reviewed manually, where possible, as a further check of the quality of the outputs of the keyword search process.

For example, using the method described above, 944 projects were categorised as being related to nanotechnology and health, approximately 27% of total nanotechnology projects. Using the keywords identified for each of the five health sub-sectors[481], a further classification could be made. In addition, nanotechnology projects relevant to health but not specifically to any of the five sub-sectors were categorised as Other. In this way, the breakdown of health nanotechnology projects was found to be: cancer 26% (CT); infectious diseases 7.8% (ID); cardiovascular diseases 5.2% (CV); neurodegenerative diseases 4.6% (ND); and diabetes (2.2%) (DB) with Other being 62% (OTH).

Where projects were classified as belonging to more than one sub-sector, a proportion of each such project was allocated to the sub-sector concerned. Thus a project relevant to cardiovascular disease and cancer would be allocated 50% to cardiovascular disease and 50% to cancer. The aim was to ensure an accurate analysis of the FP project data and to minimise double counting. The table that follows shows the number of project overlaps and the distributions of fractions of projects for the health sub-sectors.

[481] Cancer, cardiovascular disease, diabetes, infectious diseases and neurodegenerative diseases.

Table D: Distribution of projects with overlaps across health sub-sectors

	Total	CT	CV	ID	NE	DB	Other
Projects without overlaps	**883**	**196**	**23**	**48**	**24**	**11**	**581**
Projects with overlaps: fractions as allocated							
CT & ID	17	8.5		8.5			
CT & CV	12	6	6				
CT & ND	9	4.5			4.5		
CV & ID	5		2.5	2.5			
CV & ND	4		2		2		
CT & DB	4	2				2	
CV & DB	3		1.5			1.5	
ND & DB	2				1	1	
CT, ID & ND	1	0.33		0.33	0.33		
CT, ND & DB	1	0.33			0.33	0.33	
CT, CV & ID	1	0.33	0.33	0.33			
CT, CV, ID & ND	1	0.25	0.25	0.25	0.25		
ID & ND	1			0.5	0.5		
Sum of fractions	*61*	*22*	13	12	9	5	0
Total nanotechnology and health	**944**	**218**	**36**	**60**	**33**	**16**	**581**

C2 Harmonisation of data across FP6 and FP7

In order to have harmonised variables across both Framework Programmes, some names and coding of variables were required. These included the following:

i) Harmonising the participant types. The categories used in this report are presented in the table below. In the tables of top performers, if the same organisation appeared in FP6 and FP7, the FP7 code was used.

Table E: Harmonising participant type codes

Codes used	Description	FP6 Code	FP7 Code
HES	Higher or secondary education establishment	HES	HES
REC	Research organisations	REC	REC
PRC	Private commercial (excluding SMEs)	IND	PRC
SME	Small and medium-sized enterprises	SME	SME
OTH	Other including public bodies excluding research and education	OTH	OTH, PUB

ii) Introducing a classification of instruments in order to allow enhanced comparison between the varieties of instruments. The categorisation follows that of Arnold et. al (2012)[482].

[482] In their work Arnold et. al. (2012) Understanding the Long Term Impact of the Framework Programme classifies the instruments of FP4, FP5 and FP6 into four categories that are used as guidance for our classification. For FP7 the classification is done by authors of this report.

Table F: Classification of instruments

Action	Instrument	FP
Research actions	ERC Grants	FP7
Collaborative RTD actions	Integrated Projects	FP6
	Specific Targeted Research Projects	FP6
	Large-scale Integrating Project	FP7
	Small or medium-scale focused research project	FP7
	Integrating Activities / e-Infrastructures	FP7
	Collaborative project (generic)	FP7
Actions for RTD knowledge transfer	Specific Actions to Promote Research Infrastructures	FP6
	Marie Curie Actions	FP6
	Coordination Actions	FP6
	Network of Excellence	FP6
	Coordinating Action	FP7
	Marie Curie Actions	FP7
	Research Infrastructure	FP7
	Collaborative project dedicated to international cooperation partner countries (SICA)	FP7
Actions for adoption and innovation	Co-operative Research Projects	FP6
	Collective Research Projects	FP6
	Joint Technology Initiatives	FP7
	Research for SMEs	FP7
Actions to support policymaking	Specific Support Actions	FP6
	Supporting Action	FP7

iii) Participant organisations identifiers

For the FP6 and FP7 participants the following organisation identifiers were used:

- FP7: CD_ORG_ID and
- FP6: Participant Identifying Code-PIC.

If these were not available, the programme participant identifiers were used. In order to improve the comparability of the FP6 and FP7 participant identifiers, some manual matching based on organisation legal name and address data was conducted for the NT participant sample. As a result, 5,945 unique nanotechnology participants were identified.

C3 Treatment of decimals

As a general rule, the data in the tables and figures are produced by utilising the method of first summing the unrounded figures and then rounding the sum. Due to this process, some totals may not correspond with the sum of the separate figures (generally presented as limited to one decimal).

C4 Key terminology and abbreviations used

Table G: FP6 funding instrument types

Code	FP6 Type of instrument
STREP	Specific Targeted Research Projects
CA	Coordination Actions

SSA	Specific Support Actions
II	Specific Actions to Promote Research Infrastructures
IP	Integrated Projects
NOE	Networks of Excellence
MCA	Marie Curie Actions
CRAFT	Co-operative Research Projects
CLR	Collective Research Projects
I3	Specific Actions to Promote Research Infrastructures

Table H: FP7 funding instrument types

Code	FP7 Type of instrument
CP	Collaborative project
ERC	Support for frontier research (European Research Council)
MC	Support for training and career development of researchers (Marie Curie)
JTI/169	Activities under Article 169 or 171 European Treaty, Joint Technology Initiatives, Public Private Partnerships
CSA	Coordination and support action
BSG	Research for the benefit of specific groups
NOE	Network of Excellence

Table I: Organisation types

Code	Description
HES	Higher or secondary education est.
PCO	Private companies excluding SMEs
REC	Research organisations
SME	Small and medium-sized enterprises
OTH	Other (incl. public bodies and bodies with unknown organisation types)

Table J: Country codes EU28+[483].

NUTS0	Country		NUTS0	Country
AT	Austria		**LU**	Luxembourg
BE	Belgium		**LV**	Latvia
BG	Bulgaria		**MT**	Malta
CY	Cyprus		**NL**	Netherlands
CZ	Czech Republic		**PL**	Poland
DE	Germany		**PT**	Portugal
DK	Denmark		**RO**	Romania
EE	Estonia		**SE**	Sweden
ES	Spain		**SI**	Slovenia
FI	Finland		**SK**	Slovakia
FR	France		**UK[484]**	United Kingdom
EL[485]	Greece		**CH**	Switzerland
HU	Hungary		**IL**	Israel
HR	Croatia		**IS**	Iceland
IE	Ireland		**TR**	Turkey
IT	Italy		**NO**	Norway
LT	Lithuania		**ZK**	Macedonia

D Publications

Identification of publications relied on analysis of the data in the database at CWTS (the Centre for Science and Technology Studies, Leiden University, the Netherlands), data that is based on that in the Web of Science[486].

The CWTS database is organised and structured such that it allows (dynamic) field delineation and the collection of relevant publications. Hence it was possible to identify nanoscience and nanotechnology (NST) publications and, within those, to identify publications relevant to the sectors. More specifically, publications were sought within the NST group using the keywords. In addition, using the tools available at CWTS, related publications could be identified and included in the output.

Data available from the resource at CWTS included the journals in which the publications are found, the date of publication and the doi (digital object identifier). For licensing reasons, some of the data in the database at Leiden can be accessed by external parties only in aggregate form. For example, personal details of individual researchers cannot be accessed (e.g. address, email, phone number).

The report uses ISO 2-digit codes for countries. See http://www.iso.org/iso/country_codes

[483] Data was also analysed from countries outside of the EU28 namely Iceland (IS), Israel (IL), Norway (NO), Switzerland (CH) and Turkey (TR).
[484] GB is also used
[485] GR is also used
[486] http://thomsonreuters.com/en/products-services/scholarly-scientific-research/scholarly-search-and-discovery/web-of-science.html

E Patents

The patents analysed were collected from the database PATSTAT. That database includes patents from over 30 patent offices e.g. the European Patent Office, the US Patent Office and the Japanese Patent Office.

All patent offices worldwide tag nanotechnology-related patent applications using a special symbol of the International Patent Classification (IPC), namely B82Y. This special symbol is also part of the CPC (Co-operative Patent Classification). The core dataset of nano-related patents were selected using this special symbol (B82Y) from both the IPC and the CPC classifications.

All patent applications at the USPTO, the EPO and PCT (WIPO) classified as B82Y were identified in PATSTAT as well as the (simple) patent family to which they belong. From all these patent families, only patent applications at the USPTO, the EPO and PCT (WIPO) were collected. Such use of multiple patent offices helps to diminish the bias that might be caused by the so called 'home advantage' effect, i.e. the propensity of nationals to file the first patent application in their own country. By analysing across these three patent authorities a less biased overview of nanotechnology patents worldwide can be obtained.

As the patent information is being collected from more than one patent authority, and given that the same invention might be protected in more than one of these patents authorities, the (simple) patent families are used to avoid multiple counting of the same invention.

The identification of patents by sector from amongst the nanotechnology patents was based in most cases on the combination of two strategies. First, all patents including in their title and/or abstract at least one relevant keywords for a particular sector were retrieved. Second, to ensure that the patents retrieved in the first step are truly related to the sector, a number of representative IPC symbols of the sector were selected from PATSTAT[487]. For example, for the nanotechnology patents related to the health sector, the IPC symbols related to 'Pharmaceuticals' and 'Medical technology' were used. However, it was not possible to undertake this second step for all sectors as for some (e.g. manufacturing) there were no appropriate IPC symbols.

Organisations and/or individuals are listed in patent applications, these being applicants and/or inventors. This information is used in the identification of companies, universities and other research organisations active in patenting. The year of reference used is the year when the oldest priority of each patent family was applied (the closest date to the invention). The report uses ISO 2-digit codes[488] for countries.

F Products

Products were identified primarily through keyword, sector and sub-sector searches of reports and databases. This search strategy was based on a triangulation approach making use of complementing perspectives. For all perspectives the NanoData team made use of the sector specific lists of key words.

The first step was to use peer-reviewed and grey literature on products in the different sectors[489] as well as existing market reports[490]. The market reports were used to identify where nanotechnology is being applied already in products as there are many reports that appear to identify products but no product is for sale at a commercial level, being at the research stage or for very limited supply e.g. to the research community or for test purposes. These investigations were then complemented by querying web-based databases on nanotechnology products such as AZONANO[491], Nanowerk[492], the consumer products inventory of the Project on Emerging Nanotechnologies[493], the product database of understandingnano.com[494], the Nanoinformationsportal of the Österreichische Agentur

[487] PATSTAT also contains a table mapping 44 industrial sectors and the IPC classification. The linkage between technology areas and industrial sector is described in Schmoch et al (2003), "Linking Technology Areas to Industrial Sectors", final report to the European Commission, DG Research.

[488] http://www.iso.org/iso/country_codes

[489] E.g. Nanomedicine: Nanotechnology, Biology, and Medicine 9 (2013) 1–14, Hessen Nanotech (2008) Applications of Nanotechnologies in the Energy Sector.

[490] See BCC Research www.bbcresearch.com

[491] http://www.azonano.com/

[492] http://www.nanowerk.com/

[493] http://www.nanotechproject.org/cpi/

[494] http://www.understandingnano.com/nanotechnology-product-suppliers.html

für Gesundheit und Ernährungssicherheit GmbH[495], the Danish Inventory of Nanoproducts[496] and the nanowatch.de database[497]. Further sector-specific databases, such as the German database for medical practitioners and the database on European public assessment reports of the European Medicines Agency[498], were used for the identification and classification of nanotechnology related products in health, for example.

By querying databases on existing innovation policy projects, initiatives and industry platforms such as NANORA[499], the Nano-Map of the German Federal Ministry of Research[500], the database on photonic companies compiled by EPIC, the members directory of SEMI[501], and the Nano-Bio Manufacturing Consortium (USA)[502], additional enterprises active in nanotechnology sectors were identified.

A third perspective on products was developed by gathering additional information about the products from company websites identified in previous work, commercial databases and open sources of information on the web. The information was verified through additional searches (e.g. of product data sheets and company websites).

The information in the database was extensively verified. Where, for example, it was found that a product was identified but not verified, searches were made of sources including reports and company websites to check the information. Contact was also made, in some cases, directly with the company in order to ratify the existence on the market of the product. While some other databases actually state the level of known accuracy of their information (e.g. the entries in the Woodrow Wilson database are classified using a system that has categories from level 1 (extensively verified claim) to level 5 (not advertised by manufacturer – claims made only by third party)) others are not specific.

In NanoData, the aim is only to include products that can be verified.

G Other information

Several types of information are provided on the NanoData site as fixed text where data is limited or one-off. These include information on markets and wider economic data, as well as reports on environmental health and safety and information about regulation and standards.

Markets

The market data is based on available sources of information and sources of Frost & Sullivan and BCC Research, who gather their information through discussions with practitioners (e.g. company representatives) and open sources (e.g. commercial reports, web sites). The aim was to track, evaluate and measure the activities of major industry participants in the nanotechnology arena, looking at markets and usage of nanotechnology. The activities included the definition and specification of nano-materials and nano-enabled products, identification of current and upcoming products and applications, accumulating qualitative and quantitative data, identification and mapping of EU participants and last but not the least, identification and analysis of target markets.

A wide set of definitions, categorisations, data collection and forecasting methods were available. Data gathering was driven by experienced analysts and based on a data-rich portfolio of previous EU and OECD projects as well as on internal Frost & Sullivan databases and consortium members, and public database. European Patent Office[503], PRODCOM[504] and patentlens[505] databases could be used to provide in-depth information about a particular technology and to identify the key industry participants dominating the sector. Analysis of key value chains was undertaken and corroborated with other work-streams. The information thus acquired would be verified with the help of an array of primary interviews with leading technology researchers, industry experts and other active stakeholders.

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[495] http://nanoinformation.at/produkte.html
[496] http://nanodb.dk/
[497] http://www.bund.net/nc/themen_und_projekte/nanotechnologie/nanoproduktdatenbank/
[498] http://www.ema.europa.eu/
[499] http://www.nanora.eu/
[500] http://www.werkstofftechnologien.de/en/
[501] http://www.semi.org/en/Membership/MemberDirectory/
[502] http://www.nbmc.org/members-only/
[503] https://www.epo.org/searching.html
[504] http://ec.europa.eu/eurostat/web/prodcom
[505] https://www.lens.org/lens/search?n=10&q=nanotechnology&p=0

The range of primary and secondary research processes would be followed by the application of innovation diffusion tools in order to forecast probable market scenario of the future. This would also include estimating the shape of the diffusion curve and prediction of market development of nano-enabled products.

Wider economic data

External information sources such as Eurostat, OECD and WHO data sources were used to put the nanotechnology data obtained in the project into context.

For example:

- A brief overview of the energy industry was based on Eurostat data.
- The health industry overview was based on Eurostat data supplemented by reports from industry organisations (both technical (e.g. the industry association for European pharmaceutical enterprises) and financial (e.g. the European Private Equity & Venture Capital Association))

While reports on industry as a whole were available, there were found to be very few reliable reports on nanotechnology and industry. Nanotechnology databases were also explored (e.g. those of Nanowerk and Nanora).

Environmental health and safety

For the sectors in which materials were the main focus, the tool used for the environmental health and safety evaluation was the "Stoffenmanager Nano" application[506]. In summary, Stoffenmanager Nano is a risk-banding tool developed for employers and employees to prioritise health risks occurring as a result of respiratory exposure to nanoparticles for a broad range of worker scenarios. In the absence of a comparable tool for consumer exposure, it was also used for this type of exposure. Stoffenmanager Nano combines the available hazard information of a substance with a qualitative estimate of potential for inhalation exposure. Stoffenmanager Nano does not consider dermal and oral routes of exposure.

In Stoffenmanager Nano, the available hazard information is used to assign specific nanoparticles to one of five hazard bands, labelled A to E (A= low hazard, E= highest hazard). Likewise, exposure bands are labelled 1-4 (1=low exposure, 4= highest exposure).

The hazard and exposure bands are combined to yield so called priority bands ranging from low priority (=4) to high priority (=1). A high priority implies that it is urgent to apply exposure control measures or to assess the risks more precisely, and a low priority implies that it is not very urgent to apply exposure control measures or to establish the risk involved with more precision.

See also Annex: *Human health and safety.*

Regulation and standards

International, European, national and regional data sources for regulation and standards include:

European documents:

- Regulation concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) - 1907/2006(EC);
- Regulation on Medical Devices - 2012/0266(COD); and
- European Commission Recommendation on the Definition of a Nanomaterial, as well as sectoral documents such as
- Nanomaterials in the Healthcare Sector: Occupational Risks & Prevention - E-fact 73; and
- Guidance on the Determination of Potential Health Effects of Nanomaterials Used in Medical Device.

National documents:

- Decree on the annual declaration on substances at nano-scale - 2012-232 (France);
- Royal Decree regarding the Placement on the Market of Substances manufactured at the Nano-scale (Belgium); and
- Order on a Register of Mixtures and Articles that contain Nanomaterials as well as the Requirement for Manufacturers and Importers to report to the Register – BEK nr 644 (Denmark).

[506] Van Duuren-Stuurman, B., Vink, S., Verbist, K.J.M., Heussen, H.G.A., Brouwer, D., Kroese, D.E.D., Van Niftrik, M.F.J., Tielemans, E., Fransman, W., 2012. Stoffenmanager Nano version 1.0: a web-based tool for risk prioritisation of airborne manufactured nano objects. Ann. Occup. Hyg. 56, 525-541.

H Concluding remarks

This Annex outlines the main methods for the selection of data for analysis, some data sources, the aggregation of data classes in order to enable analysis (mainly for the FP projects) and the ways in which data was analysed. References are made to some of the main quality control issues.

ANNEX 2: HEALTH KEYWORDS

Below is the list of keywords used in the extraction of data and the subsequent analyses.
Each keyword is associated with either the overall sector (HT) or one of the five sub-sectors as follows:

CT: Cancer
CV: Cardiovascular
DB: Diabetes
ID: Infectious diseases
NE: Neurodegenerative disease

In the analysis, where data falls into the health sector (HT) but not into one of the sub-sectors, it is here marked as HT and usually categorised in the report as Other (OTH).

Asterisks are used to indicate that part of a word is missing. For example, the search for "diabet*" would identify data related to "diabetes", "diabetic" and "diabetics". Thus one search term was used to cover each of the words with multiple possible endings.

Alzheimer*	NE
Amyloid	NE
Amyotrophic Lateral Sclerosis	NE
Angiogenes*	CV
Antibod*	HT
Anti-Inflammat*	HT
Antimicrob*	HT
Antimicrobial Peptide	ID
Anti-Proliferative Drug*	HT
Antiviral	HT
Apoptosis	CT
Artificial Pancreas	DB
Ataxia*	NE
Atherosclero*	CV
Bioactive Glass*	HT
Biomarker	HT
Biomedical Device	HT
Brain Disease*	NE
Cancer	CT
Carcinoma	CT
Cardiovascular	CV
Chemotherap*	CT
Cholera	ID
Cisplatin	CT
Cytotoxicity	CT
Dementia*	NE
Dengue Fever	ID
Dental Implant*	HT
Dental Material*	HT
Diabet*	DB

Diagnostic Test*	HT
Disease*	HT
Doxorubicin	CT
Drug	HT
Ebola	ID
Encephalopath*	NE
ES Cell	HT
Fibroblast Growth Factor	NE
Genomic*	HT
Hepatitis	HT
Hiv	ID
Human Genom*	HT
Human Immunodeficiency Virus	HT
Huntingdon*	NE
Hyperplasia	CT
Imaging Contrast Material*	HT
Immune System	HT
Immunis*	ID
Immunisation	HT
Immunisation	HT
Immuno Modulation	HT
Immuno-Deficiency	ID
Implant	HT
Implants	HT
Infection	ID
Infectious Diseas*	ID
Inflammat*	HT
Influenza	ID
Injected Medical Device*	HT
Insulin	DB
Intraocular Release	HT
Intravitreal Delivery	HT
Iontophoresis	HT
Irradiation Equipment*	HT
Lipoprotein*	CV
Liposom*	HT
Lymp*	CT
Macrophag*	HT
Malaria	ID
Medical	HT
Medicine*	HT
Melanom*	CT
Meningeal Infiltration	NE
Metastas*	CT
Microorganism	HT
Motor Neuron	NE

Nanodrug*	HT
Nanomedicin*	HT
Nanostructured Lipid Carrier	HT
Nanothermography	HT
Nanovector	HT
Neoplasm*	CT
Neurofibrillary Tangle*	NE
Neuro-Glial Network*	NE
Neurological Phenotype*	NE
Neuronal Dysfunction*	NE
Neuropatholog*	NE
Neuroregenerati*	NE
Non-Viral System*	HT
Nutraceutical*	HT
Oncology	CT
Opthalmic	HT
Orthopaedic	HT
Orthopedic	HT
Paclitaxel	CT
Pancreatic Islet Cells	DB
Paramagnetic Immunomicell*	HT
Paramagnetic Particle*	HT
Parkinson*	NE
Peptide	HT
Perflorocarbon	CV
Perfluorocarbon	CV
Personalised Healthcare	HT
Personalised Medicine	HT
Pharmaceutical*	HT
Pharmacokinetic*	HT
Photodynamic Therap*	CT
Plaque*	CV
Pneumonia*	ID
Polyglutamine	NE
Programmed Cell Death	NE
Protein Degradation	NE
Protein Misfolding	NE
Protein Quality Control Systems	NE
Proteomic*	HT
Pulmonary	CV
Regenerative Medicine	HT
Renal Failure	DB
RNA Metabolism	NE
RNA Repeat Diseases	NE
RNA-Binding Protein	NE
Rnai	NE

Scleros*	NE
Smallpox	ID
Somatic Cell	HT
Stem Cell*	HT
Stent	CV
Surgical	HT
Theranostic*	HT
Therapeutic*	HT
Thermograph*	CT
Thrombos*	CV
Tissue Engineering	HT
Tissue Scaffold*	HT
Triclosan Delivery	HT
Tumor	CT
Tumour	CT
Typhoid Fever	ID
Vaccin*	ID
Vaccine	HT
Viral Vector*	HT
Wound Dressing	HT
Yellow Fever	ID

ANNEX 3: ABBREVIATIONS

Abbreviation	Definition
AIDS	Acquired Immune Deficiency Syndrome
ANSES	French Agency for Food Safety, the Environment and Labour
BBB	Blood-Brain Barrier
BEUC	Bureau Européen des Unions de Consommateurs
Bn	Billion
CAGR	Compound Annual Growth Rate
CBRNE	Chemical, Biological, Radiological, Nuclear and Explosive
CDE	Centre for Drug Evaluation and Research
CEN	European Standardisation Committee
CLINAM	European Foundation for Clinical Nanomedicine
CMC	Chemistry, Manufacturing and Controls
CNS	Central Nervous System
CNT	Carbon Nanotubes
COD	Co-Decision Procedure
COPD	Chronic Obstructive Pulmonary Disease
CT	Cancer-Related Health Nanotechnology
CV	Cardiovascular Disease-Related Health Nanotechnology
DB	Diabetes-Related Health Nanotechnology
DFG	Deutsche Forschungsgemeinschaft
d-MRI	Diffusion Magnetic Resonance Imaging
DNA	Deoxyribonucleic Acid
DPC technology	DNA Programmed Chemistry Technology
EACH	Executive Agency for Health and Consumers
EC	European Commission
ECDC	European Centre for Disease Prevention and Control
EEB	European Environmental Bureau
EFSA	European Food Safety Authority
EGE	European Group on Ethics Roundtables
EMA	European Medicines Agency
EoL	End of life
EPA	Environmental Protection Agency
EPR	Enhanced Permeation and Retention
ETP Nanomedicine	European Technology Platform on Nanomedicine
ETUC	European Trade Union Confederation
EU	European Union
Eurofound	European Foundation for the Improvement of Living and Working Conditions
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug and Cosmetic Act
FFDCA	Federal Food, Drug and Cosmetic Act
f-MRI	Functional magnetic resonance
FP7	Seventh European Framework Programme

Abbreviation	Definition
GMO	Genetically Modified Organism
HIV	Human Immunodeficiency Virus
HPV vaccination	Human Papilloma Virus Vaccination
HSE	Health Safety Environment
HT	Health Nanotechnology
IARC	International Agency for Research on Cancer
ID	Infectious Diseases-Related Health Nanotechnology
iMR	Interventional Magnetic Resonance
IPC	International Patent Classification
IPR	Intellectual Property Rights
ISO	International Organisation for Standardisation
JRC	Joint Research Centre
JPND	Joint Programme on Neurodegenerative Disease
MAPP	Manual of Policies and Procedures
MEMS	Micro Electro-Mechanical System
MMA	Mercaptoacetic Acid
MNBS	Micro- and Nano-Bio Systems
MR	Magnetic Resonance
MRI	Magnetic Resonance Imaging
MRS	Magnetic Resonance Spectroscopy
MRSI	Magnetic Resonance Spectroscopic Imaging
MWCNT	Multi-Walled Carbon Nanotubes
NACE	Nomenclature Statistique des Activites Economiques dans la Communauté Européenne
NANOMED	Nanomedicine ETP
NDDS	Nano Drug Delivery Systems
NE	Neurodegenerative Diseases-Related Health Nanotechnology
NGO	Non-Governmental Organisation
NH	Health Nanotechnology (in the NanoData project context)
NIH	National Institute of Health
NIR	Near Infrared
NIR-II	Near-Infrared-ii Imaging
NP	Nanoparticles
NST	Nanoscience and Nanotechnology
NT	Nanotechnology
OPS	Office of Pharmaceutical Science
OSHA	European Agency for Safety and Health at Work
OSH-Professional	Occupational Safety and Health Professional
PATSTAT	European Patent Office Worldwide Patent Statistical Database
PEG	Polyethylene Glycol
PET	Positron Emission Tomography
Poly	Polylactic-co-Glyconic Acid
ppm	Parts Per Million
QD	Quantum Dot

Abbreviation	Definition
Quantitative-PET	Quantitative Positron Emission Tomography
R&D	Research and Development
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RNA	Ribonucleic Acid
SFT	Norway Pollution Control Authority
SME	Small or Medium Sized Enterprise
SNAP	Strategic Nanotechnology Action Plan
STOA	Science and Technology Options Assessment
SWCNT	Single Walled Carbon Nanotubes
TGA	Therapeutic Goods Administration, Australia
TT	Technology Transfer
US	United States
US EPA	US Environmental Protection Agency
US NIOSH	US National Institute for Occupational Safety and Health
USA	United States of America
UV/Vis/IR	Ultraviolet / Visible / Infra-red
VC	Venture Capital
WEEE	Waste Electrical and Electronic Equipment

ANNEX 4: TERMINOLOGY

Word/phrase	Definition/explanation
Carbon Nanotubes	Allotropes of carbon with a cylindrical nanostructure.
Dendrimers	Nanostructured synthetic molecules having evenly spread branching structure originating out of a central core.
Liposomes	An artificially-prepared vesicle composed of a lipid bilayer
Nanobiosensors	Biosensor at nano-scale: measurement system for detection of an analyte that combines a biological component with a physiochemical detector
Nano-biotechnology	Intersection of nanotechnology and biology, the ways that nanotechnology is used to create devices to study biological systems, this is different from bionanotechnology
Nanocapsule	Nano-scale shells made out of a nontoxic polymer
Nanocarrier	Nano-object or objects, which are at a larger scale but which carry nanoscale payloads able to transport a diagnostic or therapeutic agent either on its surface, within its bulk structure or within an internal cavity
Nano-coatings	Applying a coating of nano-scale structures to a surface.
Nanocrystal	Nano-object with a crystalline structure
Nanodiagnostics	Application of nanotechnology in molecular diagnostics
Nanoemulsion	Nanodispersion with a liquid matrix and at least one or more liquid nano-objects
Nano-enabled	Products, systems, devices integrating, using, enabled by nanotechnology
Nano-fibres	Nano-object with two external dimensions in the nanoscale and the third dimension significantly larger
Nano-indentation	Variety of indentation hardness tests applied to small volumes. For testing the mechanical properties of materials (hardness).
Nanomaterials	Materials the single units of which is sized (in at least one dimension) between 1 and 1000 nanometres (10^−9 meter) but is usually 1—100 nm (the usual definition of nano-scale).
Nanomedicine	Medical application of nanotechnology
Nanometres	One billionth of a metre
Nano-needles	Conical or tubular needles in the nanometre size range, made from silicon or boron-nitride with a central bore of sufficient size to allow the passage of large molecules
Nanoparticle	Small object that behaves as a whole unit with respect to its transport and properties, between 1 and 100 nanometres in size.
Nanopolymers	Nanostructured polymers
Nanoproducts	Any product containing nanoparticles
Nanorod	One morphology of nano-scale objects, produced by direct chemical synthesis.
Nano-scale	Refers to structures with a length scale applicable to nanotechnology, usually cited as 1–100 nanometres, also called nanoscopic scale
Nanoscience	The study of the fundamental and functional properties of matter on the nano-scale (~10^-9m).
Nanosensor (proteomic, gold)	Any biological, chemical, or surgical sensory points used to convey information about nanoparticles to the macroscopic world
Nanoshells (plasmon)	This is also called nanoshell plasmon, is a type of spherical nanoparticle consisting of a dielectric core, which is covered by a thin metallic shell (usually gold).
Nano-specific	Refers to a system or response that is sensitive to nanomaterials
Nanostructures	An object of intermediate size between microscopic and molecular structures

Word/phrase	Definition/explanation
Nanosuspensions	Submicron colloidal dispersions of nanosized drug particles stabilised by surfactants. Nanosuspensions consist of the poorly water-soluble drug without any matrix material suspended in dispersion
Nanotechnologies / Nanotechnology	Manipulation of matter with at least one dimension sized from 1 to 100 nanometres
Nanotechnology-Based Platforms	Suit of technologies using nanomaterials, structures and objects
Nanotube	Hollow nano-fibre
Quantum Dots	A nanocrystal made of semiconductor materials that are small enough to exhibit quantum mechanical properties

ANNEX 5: ROLE OF NANOTECHNOLOGY BY DISEASE TYPE

The information in this Annex is taken from the five health sub-sector reports prepared for the Commission, one report per disease type: cancer, cardiovascular disease, diabetes, infectious diseases and neurodegenerative diseases.

CANCER

PREVALENCE AND MORTALITY RATES IN EUROPE

On a global scale, cancer was the second leading cause of death from non-communicable diseases (NCD), after cardio-vascular disease, in 2008 and 2012, as seen in the table below[507].

Deaths from non-communicable diseases globally, 2008 and 2012

	2008		2012	
	Million Deaths	% of Total NCD	Million Deaths	% of Total NCD
Cardiovascular disease	17.0	47	17.5	46
Cancers	7.6	21	8.2	22
Respiratory diseases	4.2	12	4.0	11
Diabetes	1.3	4	1.5	4
Other	5.9	16	6.8	17
TOTAL	36.0	100	38.0	100

Europe comprises only one eighth of the total world population but has around one quarter of the global total of cancer cases. It accounted for over a quarter (26%) of all deaths in Europe in 2011, with lung cancer, colon cancer and prostate cancer being the main causes of cancer death among men while breast cancer, colon cancer and lung cancer were the main three causes of cancer death among women. In 2012, an estimated[508] 2.7 million new cases of cancer were diagnosed in EU Member States 54% (around 1.5 million) occurring in men and 46% (around 1.2 million) in women, with some 3.2 million new patients per year.

The OECD has reported[509] large variations in cancer incidence across European countries with the highest incidence in 2012 in northern and western European such as Denmark, France, Belgium and Norway (over 300 new cancer cases per 100 000 population). The lowest rates were seen in Mediterranean countries such as Greece, Cyprus, and Turkey (c. 200 new cases per 100 000 population). The variations reflected both variations in the prevalence of risk factors and national policies on cancer screening reporting.

THE ROLE OF NANOTECHNOLOGY IN CANCER DIAGNOSIS AND TREATMENT

Current treatments for cancer typically focus on surgical excision, chemotherapy and radiotherapy. Their highly invasive character, toxicity and negative side-effects are driving the search for novel, cost-effective and targeted treatments. Nanoscale materials have unique thermal, optical and electromagnetic properties, differing from those at the bulk scale that can be harnessed for cancer diagnosis and therapy. The nanometre dimensions of nanoparticles are also comparable to those of biological entities such as viruses (20-450 nm), proteins (5-50 nm) and DNA (2-100 nm) making them easy to incorporate into biological systems, in this case, the human body. Nanotechnology also offers the possibility of combining imaging and drug carrier features, making for early diagnosis of diseases and revolutionising their therapy.

The vast majority of nanotechnology applications to cancer diagnosis and treatment are at early stages of development but a small number are already in use. Further detail on this will be given in the section on Products. Other examples given in the following paragraphs may not yet have left the laboratory bench.

[507] http://www.who.int/gho/ncd/mortality_morbidity/en/
[508] OECD (2014), Health at a Glance: Europe 2014 (OECD Publishing) http://dx.doi.org/10.1787/health_glance_eur-2014-en
[509] Ibid

In diagnostics, nanotechnology is already being used in the detection of cancer using biomarkers i.e. biological indicators of the presence of tumour cells in the body. These biomarkers are usually found in very low concentrations, making early diagnosis of cancer difficult. Targeting the tumour with nanoparticles can increase the fluorescence time to enable higher detection rates. By other methods, the production of biomarkers can be increased and detection made possible. Early stage detection increases the chance of recovery and makes treatments less hard on patients. In addition, nanotechnology-based diagnostics can drastically decrease the amount of sample required for analysis and is being used in high-throughput screening devices for detecting the biological signs of cancer (e.g. nanosensors, lab-on-a-chip).

Cancer imaging is being made more accurate using, for example, iron oxide or gold nanoparticles engineered with a specific coating that helps them to bind to the tumour. Being magnetic, the particles can be imaged to high resolution and accuracy, enabling the location of tumours to be established with greater precision for surgical removal. In imaging, nanoparticles are used as tracers and contrast agents and for improved endoscopes and catheters. In the future, stem cell production may be enhanced through targeting with active nanoparticles.

In therapeutics, nanotechnology is helping to target active compounds towards tumours (rather than subjecting patients to full-body or full-organ doses). Some of these compounds can also be heated using radiofrequency waves to enhance the treatment. Implantable devices can be used for localised delivery of drugs and bionanosensors to monitor the efficacy of therapies.

The development of nanotechnology-based bio-electronic sensor devices capable of detecting particular compounds within the body is an example of nanotechnology being used in combination with biotechnology and ICT for imaging purposes. In addition to detection, the device would also be capable of storing, tabulating and processing the gathered data and potentially providing a specific treatment response. A nanosensor could release a particular amount of biological or chemical compound aimed at reducing, removing or transforming a tumour.

Targeted drug delivery can be achieved by encapsulating chemotherapy drugs in a nanomaterial that deteriorates less in the body than the uncoated drug, both reducing contact of the toxic drug with healthy cells of the body and enabling the treatment to reach the tumour still in a concentrated form. Nanoparticles can themselves be injected into a tumour and activated to produce heat and destroy cancer cells locally using magnetic fields, X-rays or light. In a combination of transport and treatment, encapsulation with gold nanorods can be used firstly to carry the chemotherapy drug and secondly to enhance it when the gold nanorods are irradiated with infrared light, producing heat and helping to destroy the tumour (a treatment that is often called photodynamic therapy (PDT)).

In drug development, researchers are working at the molecular level to engineer new therapeutic agents to target and destroy cancer cells through a combination of multiple and rapidly advancing technologies, including nanotechnology. While some drugs have already reached the patient, many are at the stages of discovery, development and clinical trial.

DIABETES

PREVALENCE AND MORTALITY RATES

On a global scale, diabetes was the fourth most common cause of death from non-communicable diseases (NCD) in 2008 and 2012, as seen in the table below[510].

Deaths from non-communicable diseases globally, 2008 and 2012

	2008		2012	
	Million Deaths	% of Total NCD	Million Deaths	% of Total NCD
Cardiovascular Disease	17.0	47	17.5	46
Cancers	7.6	21	8.2	22
Respiratory Diseases	4.2	12	4.0	11
Diabetes	1.3	4	1.5	4
Other	5.9	16	6.8	17
TOTAL	**36.0**	**100**	**38.0**	**100**

[510] http://www.who.int/gho/ncd/mortality_morbidity/en/

Approximately 60 million people in the European Region have diabetes, roughly 10% each of both men and women with the disease being slightly more prevalent in men. It is becoming more common in Europe among all ages, mostly due to the effects of unhealthy lifestyles (increasing obesity, unhealthy diets and lack of exercise). Diabetes increases the risk of heart disease and stroke, can cause severe nerve damage in the feet leading to foot ulcers and possible infection and eventual limb amputation, can often damage eyesight, is one of the leading causes of kidney failure and overall it doubles the risk of death compared with the peer group without diabetes.

Type I diabetes (juvenile diabetes), is due to the autoimmune-induced total destruction of insulin-producing beta-cells in the pancreas and is currently only treatable via multiple daily injections of insulin. Early stage Type II diabetes, which is associated in part with lifestyle and obesity, can be treated by changes in diet, by increasing physical exercise, and by drugs delaying the glucose uptake in blood. The main research focus over the past decades has sought to develop improved non-invasive monitoring and insulin administration, as well as the transplantation of pancreatic islets (without immune suppression) in children with Type I diabetes.[511]

THE ROLE OF NANOTECHNOLOGY IN DIABETES

Nanotechnology may potentially be used in diagnosis (sensors) and treatments for diabetes, or a combination of the two as follows:

- Replacement of injections of insulin (for Type 1 diabetes) by non-invasive treatments such as nasal sprays and patches and the use of pills. The small size of nanoparticles can enable them to enter the body through the skin and be absorbed into the body without direct injection.
- As with many pharmaceuticals, nanocoatings are being explored as offering slow- and/or targeted- release of therapeutics.
- Novel glucose measurement methods are being developed using nanotechnology-based sensors (see box below).
- It may be possible in the longer term to combine nano-scale approaches to 'closed-loop' insulin delivery strategies which automatically release insulin in response to fluctuating blood glucose levels (BGLs), e.g. a nanotechnology based sensor of glucose levels with a dermal patch (or even a tattoo).

Currently, there are research projects[512] underway that are studying the delivery of insulin in the form of nanoparticles into the nose, or into lungs as a spray, or through the gastrointestinal tract as a pill. In addition, tests are currently being conducted on nanomaterials engineered with a glucose responsive coating; these can act as an insulin source once injected under the skin.

Diabetes monitoring using nanotechnology

1 A low-cost, reusable sensor which uses nanotechnology to screen for and monitor diabetes and other conditions, has been developed at the University of Cambridge, for use both in clinics and home settings. The sensors use nanotechnology to monitor levels of glucose, lactate and fructose in individuals with diabetes or urinary tract infections, and change colour when levels reach a certain concentration. They can be used to test compounds in urine, blood, saliva or tear fluid.

2 The sensors developed by the Cambridge team are made using laser light, which organises metal nanoparticles into alternating layers in thin gel films to produce the sensors in a matter of seconds. When glucose, lactate or fructose concentrations are high in a sample, the sensor changes colour. The exact concentration can be determined by visually comparing the colour to a reference chart, or the image can be automatically processed by a smartphone application.

3 In trials conducted earlier this year in Cambridge, the sensors showed improved performance over commercial glucose test strips read by an automated reader, while showing comparable performance state-of-the-art fully-automated glucose monitoring technology. Details were recently published in the journal *Nano Letters*. Additionally, the sensors can be produced at a fraction of the cost of commercially-available test strips. A

[511] Paragraph adapted from http://www.etp-nanomedicine.eu/public/about-nanomedicine/nanomedicine-applications/nanomedicine-to-fight-diabetes

[512] http://www.etp-nanomedicine.eu/public/about-nanomedicine/nanomedicine-applications/nanomedicine-to-fight-diabetes

single sensor would cost 20 pence to produce, and can be reused up to 400 times, compared with disposable urine test strips, which cost about 10 pence per use. The use of lasers means that the sensors can be easily manufactured at scale.

4 "These sensors can be used to screen for diabetes in resource-poor countries, where disposable test strips and other equipment are simply not affordable," said Ali Yetisen, a PhD candidate in the Department of Chemical Engineering & Biotechnology, who led the research. The team has partnered with a non-governmental organisation to deploy the technology for field use in Ghana.

Source: adapted from http://www.cam.ac.uk/research/news/nanotechnology-takes-on-diabetes
See more at: http://www.cam.ac.uk/research/news/nanotechnology-takes-on-diabetes#sthash.gwKMpNrt.dpuf

CARDIOVASCULAR DISEASE

PREVALENCE AND MORTALITY RATES

Cardiovascular disease[513] was the leading cause of death in Europe in 2011, accounting for almost 40% of all deaths in EU countries[514]. Globally, it was the primary cause of death from non-communicable diseases (NCD) in 2008 and 2012, as seen in the table below[515]. It is estimated that nearly half a trillion dollars (USD) is spent per annum on treating cardiovascular disease[516]. Central and eastern European countries report the highest mortality rates from heart attacks; Japan, Korea and France are the OECD countries with the lowest rates. Mortality rates vary by gender: across OECD countries, deaths from heart attacks in 2011 were 90% higher for men than women.[517]

Coronary artery disease (CAD) is one form of cardiovascular disease and is the leading cause of death from myocardial infarction (heart attack) in the western world and, in the United States, it results in about one-third of total deaths[518].

Deaths from non-communicable diseases globally, 2008 and 2012

	2008		2012	
	Million Deaths	% of Total NCD	Million Deaths	% of Total NCD
Cardiovascular Disease	17.0	47	17.5	46
Cancer	7.6	21	8.2	22
Respiratory Diseases	4.2	12	4.0	11
Diabetes	1.3	4	1.5	4
Other	5.9	16	6.8	17
TOTAL	**36.0**	**100**	**38.0**	**100**

THE ROLE OF NANOTECHNOLOGY IN CARDIOVASCULAR DISEASE

Nanotechnology in cardiovascular disease treatment is still largely in the research and development stage. The exact amount of use is unclear as the process of miniaturisation is ongoing and the

[513] Cardiovascular diseases (CVDs) encompass a wide variety of disorders affecting the blood vessels and heart. These conditions include angina, arrhythmias, atherosclerosis, cardiomyopathy, stroke, hypertension, myocarditis, and pericarditis. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3405780/
[514] OECD (2014), Health at a Glance: Europe 2014, OECD Publishing. http://dx.doi.org/10.1787/health_glance_eur-2014-en
[515] http://www.who.int/gho/ncd/mortality_morbidity/en/
[516] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3405780/
[517] Source: OECD (2013), "Mortality from cardiovascular diseases", in Health at a Glance 2013: OECD Indicators, OECD Publishing http://dx.doi.org/10.1787/health_glance-2013-7-en
[518] Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, et al. Heart disease and stroke statistics — 2010 update: a report from the American Heart Association. Circulation. 2010 Feb 23;121(7):e46–e215

threshold between micro- and nano-materials can be blurred in reports on products. What is clear is that nanotechnology has the potential to be used in a number of ways of detecting and of treating cardiovascular disease.

Nanotechnology has great potential for use in the healthcare system for cardiovascular disease diagnosis. As contrast agents, nanomaterials can be used to target vulnerable plaques with site, leading to possible treatments as well as diagnosis[519]. Imaging particles may permit the early identification of atherosclerosis[520], to discriminate between stable and vulnerable atherosclerotic plaques, or help in surgery in the circulatory system. Tailored therapeutic nanoparticles may in the future enable better diagnosis and treatment as diagnostic materials and treatment drugs can be brought to the centre of the health problem (possibly in an encapsulated form in a nanoparticle) to be released.

As an example of the treatment of cardiovascular disease, coronary stents (thin mesh scaffolds) have long been in use to re-open clogged blood vessels in the heart. The stent is inserted into veins around the heart and it expands once it is in place. These vascular supports are typically made of metal and coated with a polymer or other material. The coating can be used to increase biocompatibility or to introduce a pharmaceutical drug at the site of the treatment. The main purpose of the drug is to reduce the possibility of recurrence of the narrowing of the heart vessels[521]. Stents with polymer nanocoatings have been approved by the US Food and Drug Administration for clinical trials[522].

Research is also underway, for example, on the application of dendrimers (which are nanotechnology-based) in gene therapy for systemic delivery of therapeutic agents to specific targeted cells; the use of nanoparticles to target inflammatory processes in vascular diseases and enable the development of biosensors for diagnosis; and stem cell generation and manipulation by nanoparticle mediated gene transfer for the safe clinical application of gene-modified cells.

Researchers working on ICT, sensors and miniaturisation are also developing wireless wearable detector systems for people who require constant monitoring (such as those with heart disease) and imaging sensors for minimally invasive surgery.

While currently the focus is on therapies via implantable devices with targeted drug delivery, it may in the future be possible to use nanotechnology for regeneration of damaged tissue and organs via techniques including implanted bioactive materials and stem cell mobilisation.

INFECTIOUS DISEASES

PREVALENCE AND MORTALITY RATES[523, 524, 525]

Causing sixteen percent of deaths worldwide annually, infectious diseases are the leading cause of death of children and adolescents, and one of the leading causes in adults.[526] Mainly occurring in low- to middle-income countries, many of these deaths are preventable or treatable. Infectious diseases include, for example, diarrhoea, cholera, influenza, mumps, measles, hepatitis, tuberculosis, syphilis, gonorrhea and leprosy. Some figures are given below on the incidence, mortality rates and healthcare cost of just a few of these. There has been specific focus at European level on HIV/AIDS, malaria and tuberculosis in the Seventh Framework Programme for Research and Technological Development (FP7, 2007-2013).

Human Immunodeficiency Virus (HIV) has been the number one killer worldwide from a single infectious agent over recent decades, along with tuberculosis. The estimated number of global deaths in 2013 were 1.5 million each from HIV and tuberculosis. HIV/AIDS has infected over 70 million people worldwide, about 39 million of them having died. There were approximately 35 million people living with HIV at the end of 2013, an estimated 0.8% of adults aged 15–49 years worldwide. Sub-Saharan Africa remains the most severely affected location, with nearly 5% of adults living with HIV (71% of the global total). About 2 million newly-infected people were diagnosed in 2013 globally. The estimated 1.5 million deaths in 2013 was a decrease of 22% from the 2009 figure and 35%

[519] Indian J Med Res. 2015 Mar; 141(3): 285–298.
[520] Disease of the arteries characterised by the build-up of fatty tissues in the arteries
[521] http://www.degruyter.com/view/j/ntrev.2013.2.issue-4/ntrev-2013-0009/ntrev-2013-0009.xml
[522] http://celonova.com/wp-content/uploads/COBRA-PZE-US-IDE.pdf
[523] http://www.who.int/mediacentre/factsheets
[524] http://www.tbcoalition.eu
[525] WHO Fact sheet N°104, Reviewed March 2015 http://www.who.int/mediacentre/factsheets/fs104/en/
[526] www.smartglobalhealth.org

fewer than at the peak in 2005. This improvement is being caused by improved access to antiretroviral therapy (ART) and a declining incidence of HIV infection.

Tuberculosis[527] killed an estimated 1.5 million people in 2013, 360,000 of whom were also HIV positive. In the same year, 9 million people developed the disease, more than half of them in the South-East Asia and Western Pacific Regions. 4% of cases occur in the European Region and, in western European countries, result in an average of one death per 100,000 population per annum. Tuberculosis (TB) is generally regarded as preventable. TB death rate dropped 45% between 1990 and 2013. The estimated number of people falling ill with TB[528] each year is slowly declining. Incidence rates are declining fastest in the European Region, having peaked in 1999. Global TB figures are on course to meet the Millennium Development Goal target (MDG) to halve the prevalence of TB by 2015 (relative to the incidence in 1990) but in Eastern Europe and Africa the incidence of TB is not decreasing so the MDG targets will not be met. An estimated 37 million lives were saved through TB diagnosis and treatment between 2000 and 2013.

Malaria is among the deadliest of diseases[529] (660,000 deaths in 2010 and over 580,000[530] in 2013) with over 200 million new cases every year and one death from it every minute. It is most prevalent in sub-Saharan Africa, the second most affected region being South-East Asia, particularly India. Preventative and treatment methods for malaria include long-lasting insecticidal nets, indoor residual spraying and artemisinin-based combination therapies (ACT) with rapid diagnostic tests also being of importance. Drug resistance, and particularly resistance to artemisinins, is of particular concern to those aiming to prevent and treat malaria.[531]

Diarrhoea[532], a preventable and treatable disease, kills over three quarters of a million children under five every. Globally, there are nearly 1.7 billion cases of diarrhoeal disease every year, many of which could be prevented by the provision of safe drinking-water and adequate sanitation and hygiene.

Cholera was reported[533] in all regions of the world in 2013, including 22 countries in Africa, 14 countries in Asia, 8 in the Americas and 2 in Europe. Currently it is estimated that there are 3-5 million cases of cholera every year and 1-200,000 deaths result. 65% of those deaths typically occur in 17 countries on the African continent and 30% occurring across the Americas, the Dominican Republic and Haiti.[534]

Influenza is a very common disease with constantly changing strains. A study of estimated deaths from influenza in the United States covering the 31 flu-seasons from 1976 to 2007 reported[535] death figures of between 3,000 and 49,000 with, in general, 90% of deaths occurring in the age range of 65 and over in industrialised countries. Worldwide, annual flu epidemics cause about 3 to 5 million cases of severe illness, and result in 250 000 to 500 000 deaths. For EU/EEA countries, a rough estimate gives an average of 38,500 influenza attributable deaths per annum[536] in a typical year. In Europe, the impacts on healthcare costs and productivity are significant. It has been estimated[537] that "the implementation of a 100% vaccination rate programme for all risk groups in France, Germany, Italy, Spain and UK would require an additional EUR 1.52 billion but would result in estimated savings of EUR 39.45 million of reduced primary care visits and further savings of EUR 1.59 billion in reduced hospitalisations respectively in these countries".

Antimicrobial Resistance (AMR): For the past 70 years, antimicrobial drugs, such as antibiotics, have been successfully used to treat patients with bacterial and infectious diseases. Over time, however, many infectious organisms have adapted to the drugs designed to kill them, making the products less effective. To address this growing problem, research & development on many aspects of antimicrobial (drug) resistance is being carried out, including basic research on how microbes develop resistance, new and faster diagnostics, and clinical trials designed to find new vaccines and

[527] http://www.who.int/tb/publications/global_report/en/
[528] About one third of the global population has latent TB but is unaware of it and does not pass it on to others.
[529] http://www.who.int/malaria
[530] The uncertainty ranges are large: 367,000 to 755,000. http://www.who.int/mediacentre/factsheets/fs094/en/
[531] http://www.who.int/malaria/media/world_malaria_report_2012_facts/en/
[532] http://www.who.int/mediacentre/factsheets/fs330/en/
[533] http://www.who.int/wer No. 31, 2014, 89, 345-356
[534] http://www.who.int/mediacentre/factsheets/fs107/en/
[535] http://www.cdc.gov/flu/protect/keyfacts.htm
[536] http://www.ecdc.europa.eu/en/activities/sciadvice/_layouts/forms/Review_DispForm.aspx?List=a3216f4c-f040-4f51-9f77-a96046dbfd72&ID=394
[537] Vaccine, Volume 24, Issues 47–48, 17 November 2006, Pages 6812–6822, http://www.sciencedirect.com/science/article/pii/S0264410X06008954

treatments effective against drug-resistant microbes. The World Economic Forum has proposed that AMR be added to the global risk register, and the WHO has highlighted the serious implications of AMR for global public health[538]. The problem of AMR extends beyond human health to animals.

THE ROLE OF NANOTECHNOLOGY IN INFECTIOUS DISEASES

Nanotechnology provides the opportunity to address microbes and our immune systems at a molecular level. While there are many potential applications for nanotechnology in the area of infection and immunity, some of the earliest and most promising developments have been in the development of antimicrobial agents and new vaccines.[539]

Antimicrobial Agents: Nanoemulsions are oil-in-water droplets ranging from 200-600 nm^2. These are high-energy droplets, thermodynamically-driven to fuse with lipid-containing organisms. These antimicrobial agents can be used in wound irrigation and decontamination of high-risk surfaces (for example, in hospitals). Studies have shown these agents to be effective against bacteria (E. coli, salmonella, S. aureus), viruses (HIV, herpes), and fungi (candida). Nanoparticles are also used to deliver antimicrobial agents. Research in this area began in the early 1990s, and has since expanded to encompass treatment of many intracellular infections, including fungal and parasitic infections, Listeria, Salmonella and Tuberculosis. Nanoparticle carriers can be metallic, lipid-based, polymer-based or biological (resembling a virus).

Vaccine Development: The nano-engineering of vaccines enables the creation of better adjuvants and vaccine delivery systems. Currently, nanoparticles are being used in the design of nasal and transcutaneous vaccines. Some of the promising nasal vaccines under development include vaccines for: parainfluenza, hepatitis B, measles, yersinia pestis, and HIV. Particular attention is being paid to the HIV vaccine. Since HIV targets immune cells in an unusual way, standard approaches to an HIV vaccine have been met with limited success. Current transcutaneous particle-based vaccines are made of naturally occurring "particles" and can vary in quality from batch to batch and induce adverse events.

With clinical applications of nanoemulsions and nanoparticle vaccines already in use, it is not difficult to imagine other potential applications of nanotechnology in immunology. Drug delivery systems designed to interact with tissue in specific locations and times are currently being used in engineering. These systems should allow for more accurate targeting of therapeutic agents – allowing greater therapeutic effects through increased activity, and decreased adverse effects. These medications take advantage of the ability to control molecular structure to allow for enhanced activity.

The role of nanotechnology in infectious diseases further includes reducing infection in infectious diseases includes reducing infection transmission by using super-clean, nano-textured bactericidal surfaces. It can also potentially be used for imaging to trace the path of infection and to help in the safe implanting of diagnostic and therapeutic materials within the body.

Through the use of nanotechnology, sensors are being made more sensitive and the time for diagnosis (and therefore treatment) is being reduced, one current application of nanotechnology to infectious diseases. Time critical diagnostic information can be obtained more rapidly and immediate treatment given, with monitoring with immediate feedback becoming a short-term research and development objective (e.g. for bacterial or viral infections).

NEURODEGENERATIVE DISEASES – PREVALENCE AND MORTALITY RATES

NEURODEGENERATIVE DISEASES IN THE EU[540]

Europe has a rapidly ageing population. Currently, 16% of the European population is over 65, and this figure is expected to reach 25% by 2030. Neurodegenerative diseases such as Alzheimer's and Parkinson's disease are debilitating and largely untreatable conditions that are strongly linked to age.

Dementias are responsible for the greatest burden of disease with Alzheimer's representing approximately 60-70% of cases. Alzheimer's disease and related disorders affect over 7 million

538 http://www.who.int/drugresistance/documents/surveillancereport/en/
539 Applications of Nanotechnology in Infectious Disease. Pencilla Lang and Jenny Shu. UWO Medical Journal, 2014 Vol 78, Issue 2
540 Adapted from: http://www.neurodegenerationresearch.eu and http://ec.europa.eu/health/major_chronic_diseases/diseases/brain_neurological/index_en.htm

people in Europe, and this figure is expected to double every 20 years as the population ages.

It currently costs approximately EUR 130 billion per annum to care for people with dementia across Europe, making age-related neurodegenerative diseases one of the leading societal challenges faced by EU Member States – and not only from a cost perspective. Alzheimer's disease is particularly expensive to manage due to its insidious onset, its ever-increasing levels of disability and the length of time over which the condition extends itself (average duration: 2 to 10 years).

Existing treatments for neurodegenerative diseases are very limited, and only treat the symptoms, rather than addressing the cause. In addition, no new drug treatment for Alzheimer's disease has been approved in the past five years.

PREVALENCE AND COST OF DEMENTIA IN OECD COUNTRIES[541]

Clinical symptoms of dementia usually begin after the age of 65, and the prevalence increases markedly with age. The disease affects more women than men. In Europe, 14% of men and 16% of women aged 80-84 years were estimated as having dementia in 2009, compared to less than 4% among those under 75 years of age. For people aged 90 years and over, the figures rise to 31% of men and 47% of women. A similar pattern is observed in Australia. Early-onset dementia in people aged younger than 65 years is rare; they comprise less than 2% of the total number of people with dementia.

The direct costs of dementia account for a significant share of total health expenditure in OECD countries, greater than the direct costs related to depression and other mental disorders such as schizophrenia. In the Netherlands, dementia accounted for nearly 6% of overall health spending in 2007. Most of these costs were related to caring for people with dementia in nursing homes, but part of the costs were also related to home-based care and a smaller proportion for hospital-based care. In Germany, dementia accounted for 3.7% of total health expenditure in 2008, with most of the costs also allocated for care in nursing homes.

THE ROLE OF NANOTECHNOLOGY IN NEURODEGENERATIVE DISEASES

The efficacy, cellular uptake and specific transport of drugs and/or imaging agents to target organs, tissues and cells are common issues in the diagnosis and treatment of different disorders. In the case of neurodegenerative diseases, they represent complex problems, since brain-targeting remains a still-unsolved challenge in pharmacology, due to the presence of the blood–brain barrier, a layer of cells that prevents unwanted substances from entering the brain. Engineered nanomaterials, objects with dimensions of 1–100 nm, are providing interesting biomedical tools potentially able to solve these problems, thanks to their physico-chemical features and to the possibility of multi-functionalisation, allowing to confer them different features at the same time, including the ability to cross the blood–brain barrier[542].

Diagnosis and treatment of neurodegenerative diseases using nanotechnology includes the potential use of semi-invasive devices (such as micro-needles) for drug delivery, implantation of advanced neurostimulators using nano-enhanced imaging techniques and the possibility of combining imaging and drug carrier features, making for early diagnosis and targeted therapy. It may be suitable for neuroprotection; neural regeneration and drug delivery systems

One area of particular interest, as mentioned above, and currently at the research level, is the development of nanoparticles able to cross the blood–brain barrier to enable diagnosis of and therapy for neurodegenerative diseases. This and other new applications, if they come to fruition, can help to treat patients at an early stage thereby optimising their healthy life years and ability to manage on their own.

Different approaches have been tried to overcome the blood–brain barrier. Currently, the most promising strategies are those based on nanomaterials designed to interact with the blood–brain barrier cells at molecular level, exploiting the existing physiological mechanisms of transport, without interfering with the normal function of the barrier itself. Receptor and adsorptive-mediated transcytosis are the most encouraging mechanisms to facilitate the transcellular transport of nanomaterials from the blood to the brain.

Nanotechnology-based developments aim for Alzheimer's disease, Parkinson's disease, prion

541 OECD (2013), "Dementia prevalence", in Health at a Glance 2013: OECD Indicators, OECD Publishing. http://dx.doi.org/10.1787/health_glance-2013-74-en

542 Nanotechnology for neurodegenerative disorders, Re, Gregori and Masserini, Maturitas 73 (2012), 45-51. doi:10.1016/j.maturitas.2011.12.015

disease, and Amyotrophic Lateral Sclerosis (ALS). In addition, nanotechnology for neuroprotection and neuronal tissue regeneration is under research. A challenge will be the use of nanomaterials for combined therapy and diagnosis strategies (theranostics). For this purpose, the most suitable NP are currently magnetic ones, that may be utilised for MRI, targeted drug and gene delivery, tissue engineering and cell tracking, for their unique ability to be guided by an external magnetic field.

Nanotechnology has the potential for the better understanding of the root cause molecular mechanisms that lead to neurodegenerative diseases (such as Alzheimer's disease) through the use of atomic force microscopy, single molecule fluorescence microscopy and NanoSIMS microscopy. It has also been proposed that nanotechnology can be used as a tool for early diagnosis (because of its ability to detect ultra-low concentration of bio-markers) via bio-barcode assays, localised surface plasmon resonance nanosensors, quantum dot and nanomechanical cantilever arrays.[543] Nanotechnology may in the future be used as neuroprotections against oxidative stress and anti-amyloid therapeutics, and for neuroregeneration and drug delivery beyond the blood-brain barrier. A complete cure for some neurodegenerative diseases may become feasible via a combination of nanotechnology and some other novel approaches, like stem cell technology. [544]

In terms of drug delivery, more personalised treatment will become possible if nanotechnology, biotechnology and engineering can be combined to measure a patient's genetic predisposition to side effects and their drug response characteristics. Further in the future, nanotechnology may contribute to site-specific delivery of neuro-active molecules and techniques for regeneration of the central nervous system.

Nanotechnology can also offer solutions for the carers of people suffering from neurodegenerative diseases. Less intrusive and miniaturised devices can also offer enhanced acceptability in patients, an advantage perhaps particularly relevant to people suffering from neurodegenerative diseases and other neurological conditions.

[543] http://trialx.com/curetalk/2013/02/nanotechnology-based-developments-for-treatment-prevention-and-diagnosis-of-alzheimers-disease/

[544] Nanotechnology solutions for Alzheimer's disease: advances in research tools, diagnostic methods and therapeutic agents, Nazem and Mansoori, J Alzheimers Dis. 2008 Mar;13(2):199-223. http://www.ncbi.nlm.nih.gov/pubmed/18376062

ANNEX 6: ADDITONAL INFORMATION ON MEMBER STATE POLICIES AND PROGRAMMES

In addition to actions at the level of the whole of the European Union, many countries have developed strategies and action plans and funded programmes and projects. Some of these are identified and outlined below, by country.

The aim in this section is to give a flavour for the policies and programmes that are or have been in place for nanotechnology at Member State level, in the wider context of national strategies for science, technology, research and development. As it focusses on targeted initiatives for nanotechnology, not all EU28 countries are included.

This section has been prepared from existing data sources (e.g. Member State government and agency reports and web sites, European Commission sources (such as ERAWATCH/RIO[545]), evaluation reports). While efforts have been made to use the most up-to-date sources, it cannot be guaranteed that all information is current.

AUSTRIA

In Austria, the two main ministries involved in the funding of research and development (R&D) are the Federal Ministry of Science and Research (BMWF)[546] and the Federal Ministry for Transport, Innovation and Technology (BMVIT)[547]. The largest share of direct support for R&D is channelled through three funding agencies: The Austrian Science Fund (FWF)[548] that focuses on funding academic research; the Austrian Research Promotion Agency (FFG)[549] specialising in funding applied industrial research and the co-operation between the higher educational sector and industry; and the Austria Economic Service (AWS)[550] that is mainly active in support programmes for SMEs.

In 2004, the Federal Ministry for Transport, Innovation and Technology launched the "Austrian NANO Initiative" and in 2010, the "**Austrian Nanotechnology Action Plan**"[551] was adopted by the Federal Government. The NANO initiative was a response to regional activities in the Austrian Bundesländer (such as NanoNet Styria [for more information, see later in this Annex]) that sought to identify existing competences and to formulate potential themes for large-scale co-operative projects.

An important motivation in the establishment of such a national research programme was the expectation that its creation would strengthen the national research community in specific fields thereby better linking them to international communities. At that time, most Austrian peer countries (Germany, Switzerland, UK, and Finland), as well as the European Framework Programmes, were using the label nanotechnology for framing focused research programmes.

The NANO initiative aimed to address the following issues: What would be the best way for Austria to harness the opportunities in nanotechnology (for instance, in environmental and energy technology and new resource-saving products or for small- or medium-sized enterprises)? How could Austria contribute to ensuring the safety for its citizens of nanotechnology applications?

NANO had the following objectives: to increase networking among actors so as to achieve critical mass; to open up ways to exploit the benefits of nanotechnology for industry and society; and to ensure proper support for qualified personnel. To achieve these objectives, it had two programme action lines:

1. National co-operative RTD Projects (Research and Technology Development in Project Clusters (RPCs) and
2. Transnational co-operative RTD Projects (Research and Technology Development in Transnational Projects).

A key aspect of the **Nanotechnology Action Plan** to implement the NANO initiative was to strengthen communication and the dissemination of information to specific target groups, particularly the interested public. Information on the fundamentals, opportunities and risks of nanotechnology

[545] https://rio.jrc.ec.europa.eu/
[546] http://www.en.bmwfw.gv.at/
[547] https://www.bmvit.gv.at/en/
[548] https://www.fwf.ac.at/en/
[549] https://www.ffg.at/en
[550] http://www.awsg.at/
[551] https://www.bmlfuw.gv.at/dam/jcr:00058164-0320-4544-b6a4-320325dcfd86/Austrian%20Nanotechnology%20Action%20Plan.pdf

was provided to the public through an information portal for nanotechnology. A primary objective was to engage the public in the process of drawing up and implementing a Nanotechnology Action Plan[552], which underwent public consultation via the Internet in Autumn 2009, as did the Implementation Report in November 2012. The feedback received was published online and taken into account in the follow up to the Action Plan and Implementation Plan respectively.

One of the central measures of the Austrian Nanotechnology Action Plan was the establishment of a programme for the environment, health and safety (EHS). NANO EHS was established to provide targeted funding for environment- and health-related research into assessing the risks of synthetic nanomaterials.

NANO was implemented from 2004 to 2011 by the Austrian Research Promotion Agency (FFG)[553] and, in total, nine large-scale co-operative projects were funded across a wide array of sectors such as photonics, nanomedicine, and nanomaterials. Since 2012, support for nanotechnology R&D has been provided through the thematic programmes of FFG.

In addition to the above governmental actions, an Austrian network was created, **BioNanoNet**[554]**,** combining a wide range of expertise in numerous disciplines of medical and pharmaceutical research in nanomedicine and nanotoxicology. The BioNanoNet Association is also the owner of BioNanoNet Forschungs GmbH. Working across both biotechnology and nanotechnology, and visible at international levels, BioNanoNet addresses the scientific areas of:

- Nanotoxicology,
- Sensor technology
- Health and safety, including (nano-) medicine and nanosafety.

The BioNanoNet coordinates **EURO-NanoTOX**[555], which is an open virtual centre and national platform. EURO-NanoTOX is co-funded by the Federal Ministry of Science and Research (BMWF). It elaborates strategies to conduct standardised toxicological in-vitro as well as in-vivo methods on nanostructured materials. Its main focus is on human nanotoxicology and human risk assessment.

Regional Nanotechnology initiatives:

Wirtschaftsstrategie Steiermark 2020 (2011)[556]: Styria's Economic Strategy 2020 is a successor to the State Government's previous economic strategy 2006. The 2006 strategy identified so-called economic and technological strong-points ("Stärkefelder") of the region, on which innovation policy activities were focused: material sciences; mechanical engineering/automotive and transport technologies; chemical and process engineering; human technology; information and communication technologies; environmental technologies; energy; building services engineering (including timber construction); nanotechnology; computer simulation and mathematical modelling. The 2011 strategy bundles activities in these fields under three major leading themes: i) mobility, ii) eco-technology, and iii) health technology. The central aim is to focus on future activities and to establish Styria as a "European benchmark for the structural change towards a knowledge based production-society".

BELGIUM

Since its two regions play a central role in Belgian policy making, the main nanotechnology activity in the country is carried by the regional government of Flanders, with a number of institutions working in the area of nanotechnology.

Strategische onderzoekscentra[557] **(SOC's)** is a strategy of the Region of Flanders which gives institutional funding to four Strategic Research Centres that collaborate with the academic and business worlds. Each of the institutes have their own specific focus.

- Imec[558] is a leading European independent research centre in micro- and nanoelectronics, *nanotechnology,* design methods and technologies for ICT systems. It carries out research that

[552] http://www.sozialministerium.at/cms/site/attachments/6/1/7/CH2120/CMS1371046721712/umsetzungsbericht_2012_en.pdf
[553] https://www.ffg.at/en
[554] http://www.bionanonet.at/about-bionanonet
[555] http://www.bionanonet.at/about-nanotoxicology?lang=english
[556] http://www.wirtschaft.steiermark.at/cms/beitrag/10430090/12858597
[557] http://www.ewi-vlaanderen.be/wat-doet-ewi/excellerend-onderzoek/strategische-onderzoekscentra
[558] http://www2.imec.be/be_en/home.html

runs three to ten years ahead of industrial needs. The world's top integrated device manufacturers, equipment and material suppliers, system houses and electronic design automation (EDA) vendors participate in the research conducted there. Work at Imec has a strong connection to nanotechnology given its use in electronics and as the next generation technology for electronics and ICT.

- VIB[559], the Flanders Institute for Biotechnology, is an autonomous entrepreneurial research institute that conducts strategic basic research in life sciences, including molecular biology, cell biology, developmental biology, structural biology, genetics, biochemistry, microbiology, genomics and proteomics. It is considered to be a leading European centre. Much of its work is at the *nanoscale*.
- VITO[560], the Flemish Institute for Technological Research, is an independent contract research and consulting centre. It converts the latest scientific knowledge and innovative technologies into practical applications, both for public authorities and industry. The research centre operates in the fields of energy, environmental and material technology, in industrial product and process technologies and in remote sensing, with *nanotechnology* applications.
- iMinds[561] is an independent research institute that stimulates innovation in information & communication technology (ICT) and broadband. This research is interdisciplinary and demand-driven, and takes place in close collaboration with businesses and governments, both local and international. Its aim is to provide solutions to complex problems and thus help meet society's future challenges.

In 2003, the Regional Government of Wallonia launched a nanotechnology program in order to support research projects in that field which led to the creation of **NanoWal**[562], a structure to favour interactions between actors in nanotechnology field. Nanowal became a non-profit organisation in 2009.

THE CZECH REPUBLIC

In 2005, the Academy of Sciences of the Czech Republic approved the programme "**Nanotechnology for the Society**" with the objective of achieving progress in the development of research and utilisation of nanotechnologies and nanomaterials within Czech society[563]. It included four different sub-programmes in the areas of: nanoparticles, nanofibres and nanocomposite materials; nanobiology and nanomedicine; nano-macro interface; and new phenomena and materials for nanoelectronics, with specific priorities in all of them. The programme was planned to end in 2012.

Other general programmes with a less specific mention to nanotechnology came from the Grant Agency of the Czech Republic, the Ministry of Education, Youth and Sports and the Ministry of Industry and Trade.

In the National Research, Development and Innovation Policy document of the Czech Republic in 2009-2015[564], nanotechnology is addressed under the **Materials Research** priority, where it is set as an area to be supported by national budget in order to increase the global competitiveness of the Czech economy through products with high added-value.

DENMARK

In Denmark, the Ministry of Higher Education and Science[565] has the main responsibility for research and innovation policy.

In the period from 2001 to 2004, steering groups set up by the Danish government carried out a Technology Foresight pilot programme. The aim of the programme was to carry out eight foresight studies in the three-year period, and to identify issues of strategic importance for science, technology, education, regulation and innovation policy in these areas. The foresight studies included bio- and health care technologies, and ICT (pervasive computing, future green technologies, hygiene and nanotechnology, especially nanomedicine[566]). The last phase of the foresight programme was

[559] http://www.vib.be/en/Pages/default.aspx
[560] https://vito.be/en
[561] https://www.iminds.be/en
[562] www.nano.be/
[563] http://www.csnmt.cz/getfile.php?type=file&IDfile=24
[564] http://www.vyzkum.cz/FrontClanek.aspx?idsekce=1020
[565] http://ufm.dk/en
[566] Danish Nano-science and Nano-technology for 2025, Foresight Brief No. 032

closely linked to the establishment of the Danish National Advanced Technology Foundation[567] for the development of generic technologies of future importance such as ICT, biotechnology and nanotechnology.

The Action Plan "Strategy for Public-Private Partnership on Innovation", launched in 2003, focused on how to improve co-operation between education, research and trade/ business. The goal was for more enterprises, especially SMEs, to have faster and easier access to knowledge. In 2004, the Ministry of Science, Technology and innovation issued **the Technology Foresight on Danish Nanoscience and Nanotechnology – Action Plan[568]** as a basis for Danish policy on research, education and innovation in the area. The vision was to raise awareness of and promote the utilisation of nanotechnology in Denmark.

In 2003, on foot of the above developments, the Ministry of Science, Technology and innovation published a call for the establishment of high-tech public-private networks in bio, nano and information technology. The goal was to create stable collaboration patterns between companies and knowledge institutions to increase knowledge transfer to, and use in, private industry. The funding was to be used to finance networking. In the first round (in 2004) the Ministry provided seven networks with a budget of EUR 3.7 million (around EUR 0.5 million each). Amongst the networks was NaNet which, (together with Nano Øresund) became one of the two most important Danish nanotechnology networks. NaNet's mission was to create platforms for the exchange of information on nanotechnology, and to facilitate its utilisation on all levels of society, from research and education to industrial application and development.

Between 2005 and 2010, EUR 116 million was allocated to strategic research centres, research alliances and research projects, EUR 62 million being for nanotechnology, biotechnology and ICT. Among the strategic research centres funded under the programme is a Centre for Nano-vaccines[569].

Since 2009, the Danish National Advanced Technology Foundation has channelled funding for projects in high-tech sectors, such as nanotechnology, biotechnology and ICT.

Support for nanotechnology research has been managed through a number of sources. The Danish Council for Strategic Research, part of the Danish Agency for Science, Technology and Innovation is one of these, although the council itself did not authorise funds for research, dependent instead on the Programme Commission, which covers Nanoscience, Biotechnology and IT (NABIIT). The Strategic Research Programme for the Interdisciplinary Applications of NABIIT technologies supported the establishment of networks and research initiatives. Research support also came from the Danish National Research Foundation, the Danish Ministry of the Interior and Health's inter-ministerial working group on Nanotechnology and Human Health, and the Danish National Advanced Technology Foundation. Latterly, also under the Danish Council for Strategic Research, the Programme Commission on Strategic Growth Technologies has had annual calls of total annual value approximately EUR 10 million for research projects on nanotechnology, biotechnology and information- and communication technology. In 2013, The Danish government and five political parties decided to revise the research and innovation system, agreeing to merge the Danish National Advanced Technology Foundation, the Danish Council for Strategic Research and the Danish Council for Technology and Innovation into a new innovation foundation. Thus, the new organisation Innovation Fund Denmark[570] (IFD), has been the responsible body since 2014.

FINLAND

The main focus areas of public research and development (R&D) funding in Finland are energy and the environment, health and well-being, the information and communications industry, the forest cluster, and metal products and mechanical engineering. Nanotechnology is treated as a technology to be applied across all these focus areas. Finland spends approximately 3.5 % of its gross national product on (R&D). Exploitation of research results being seen as even more important than the amount of investment, the Finnish innovation environment seeks to promote the exploitation of scientific and technological results in Finnish companies.

The main research policy decisions are drawn up in the Science and Technology Policy Council of

[567] http://www.tekno.dk/about-dbt-foundation/?lang=en
[568] http://ufm.dk/en/publications/2004/technology-foresight-on-danish-nanoscience-and-nanotechnology
[569] http://www.nano-vaccine.org/
[570] http://innovationsfonden.dk/en; In 2015, IFD had an annual budget of DKK 1.6 billion, but their budget is expected to decrease to DKK 1.47 billion in 2016. The total budget for innovation funds areas was over DKK 2 billion in 2010, so a significant loss of funding took place during the last 5 years. http://innovationsfonden.dk/da/nyhed/innovationsfonden-investerer-ogsaa-i-forskernes-gode-ideer

Finland chaired by the Prime Minister. The principle instruments in the implementation of the policy are the funding organisations working under the ministries. Tekes, the Finnish Funding Agency for Technology and Innovation operates under the remit of the Ministry of Trade and Industry while the Academy of Finland is governed by the Ministry of Education. Nearly 80% of all public research funding is channelled through these two organisations.

The **first Finnish nanotechnology programme** was financed jointly by Tekes and the Academy of Finland in 1997–1999[571]. Its objective was to build know-how, multi-disciplinary infrastructure and linkages between fundamental and applied research. The programme also established a new form of co-operation using joint funding between Tekes and the Academy of Finland. The total value of the programme was EUR 7 million (Tekes EUR 4m, the Academy of Finland EUR 3 m).

FinNano, the Finnish nanoscience and nanotechnology programme, was established in 2005. The programme was co-ordinated jointly by Tekes and the Academy of Finland and covered the whole innovation chain from basic research to commercial products. The aim of the programme was to strengthen Finnish nanotechnology research in selected focus areas and to accelerate the commercial development of nanotechnology in Finland. The key objective was to boost internationally recognised high-level research and competitive business based on nanotechnology.

In addition to FinNano, the Ministry of Education provided funding to develop nanoscience education and infrastructure in Finnish universities and the Nanotechnology Cluster Programme was initiated in 2007 with the Centre of Expertise Programme. In total, Finnish public funding for nanotechnology during 2005–2010 was approximately EUR 235m.

In practice, the FinNano programme was executed in two parts: Tekes' FinNano – Nanotechnology Programme (2005–2009) and the Academy of Finland's FinNano – Nanoscience Programme (2006–2010). The Programme had a total value of approximately EUR 70m, including EUR 25m in research funding and EUR 20m in corporate financing from Tekes. The original programme plan defined three main focus areas:

1) Innovative nanostructure materials;
2) Nanosensors and nanoactuators; and
3) New nanoelectronics solutions.

In 2007, the aims of the programme were redefined as being for:

- Society: Renewal of industry clusters and production, environment and safety;
- Applications: Electronics, forest cluster, chemical sector, health and well-being; and
- Technologies: Nanostructured and functional materials, coatings and devices; Measurement methods, production and scalability.

According to a programme's interim evaluation in 2008, the main successes of FinNano were to activate companies in research and product development, to map all the existing nanotechnology infrastructure and to create cross-cutting networks of nanotechnology professionals.

In 2011, the final report on FinNano was published, showing the results of the Programme[572]. According to that report and an independent evaluation by Gaia Consulting Ltd., all the Finnish nanotechnology programmes succeeded and fulfilled their objectives, which ranged from capturing knowledge in nanoscience and technology to boosting Finnish nano research and business. The next steps in the development of nanotechnology for industry in Finland were recommended to be achieved by other means. These included measures to enhance technology transfer, encouragement of entrepreneurship, and seed funding and basic research funding based on problems and not in disciplines.

In more recent years, Finland has therefore stopped identifying nanotechnology as a separate area for funding, opting to fund it under general R&D funding programmes and actions to enhance technology transfer and commercialisation by industry in Finland.

FRANCE

In 1999, the "**French Research Network in Micro and Nano Technologies**" (RMNT) was created for the purpose of strengthening and reorganising micro- and nano research and aligning it with the private sector.

In 2003, a **network of major technology centres** was created, linking together the facilities at

[571] http://www.tekes.fi/globalassets/julkaisut/research_and_technology.pdf
[572] http://www.tekes.fi/globalassets/julkaisut/finnano_loppuraportti.pdf

the following organisations:

- *CEA-LETI*[573] in Grenoble (centred in Minatec);
- The *Laboratoire d'Analyses et d'Architectures des Systemes*[574] (LAAS) in Toulouse ;
- The *Laboratoire de Photonique et de Nanostructures*[575] (LPN) in Marcoussis ;
- *The Institut d'Électronique Fondamentale*[576] *(IEF) Orsay,* in Minerve; and
- The *L'Institut d'Electronique, de Microélectronique et de Nanotechnologie* [577] (IEMN) in Lille.

The creation of this network was supported by a total subsidy of EUR 100 million for the period 2003 to 2006.

Launched in 2003 to fund fundamental research, France's national N**anosciences Programme** was co-ordinated by the Ministry of Research in co-operation with the CNRS (National Scientific Research Centre), the CEA (French Atomic Energy Commission) and the DGA (General Delegation for Weaponry).

In 2005, the French National Research Agency (ANR) was established to assume responsibility for the funding and organisation of all national R&D projects, in order to improve co-ordination. Today, national nano research is funded within the national programme for nanosciences and nanotechnologies (**PNANO**[578]) under the ANR. The budget of the ANR for 2005 was EUR 539m, EUR 35.3m of which was dedicated to PNANO. The ANR has funded research projects in nanosciences and nanotechnologies mostly through the following research programmes:

- Non-thematic programmes (called "programmes blancs")
- Nanotechnologies and Nanosystems programmes P2N.
- Additional programmes, which are more specific to a given topic, such as those on hydrogen storage and fuel cells or on home photovoltaics.

A EUR 35 billion economic stimulus package **Investissements d'Avenir**[579] (Investments for the Future) was launched at the end of 2009. Within that context and since 2011, nano-bio-technology has been one of the priority areas for funding under the ANR, with a particular focus on health and environmental research. The package aims to support scientific research, accelerate its transfer to a pilot stage and to consolidate knowledge about toxicology and nanomaterials, the programme is funding therapies, imaging, diagnostics and medical devices base on nanotechnology and biotechnology.

GERMANY

As far back as 1998, the Federal Ministry of Education and Research (BMBF) increased collaborative project funding for nanotechnology. In addition, an infrastructure plan was put in place in the form of the establishment of six competence centre networks. The measures were implemented two years before the USA began its national nanotechnology initiative and four years before the European Union's comparable measures under the Sixth Framework Programme.

In 2004, the German Innovation Initiative for Nanotechnology - "**Nanotechnology Conquers Markets"**[580] was launched and presented to the public. On the basis of the White Paper presented at the nanoDe congress in 2002 and intensive discussions with representatives from business and science, the BMBF's new approach to nanotechnology funding was based on Germany's highly-developed and globally competitive basic research in sciences and technology and primarily aimed to open up the application potential of nanotechnology through research collaborations (leading-edge innovations) that strategically target the value-added chain. The main elements of the strategy were to open up potential markets and boost employment prospects in the field of nanotechnology. Five leading-edge innovation programmes were funded initially:

- NanoMobil, for the automotive sector;

[573] http://www-leti.cea.fr/en/
[574] https://www.laas.fr/public/
[575] http://www.lpn.cnrs.fr/fr/Commun/
[576] http://www.ief.u-psud.fr/
[577] http://exploit.iemn.univ-lille1.fr/
[578] http://www.agence-nationale-recherche.fr/suivi-bilan/historique-des-appels-a-projets/appel-detail1/programme-national-en-nanosciences-et-nanotechnologies-pnano-2005/
[579] http://www.gouvernement.fr/investissements-d-avenir-cgi
[580] http://d-nb.info/97392179x/34

- NanoLux, for the optics industry;
- NanoforLife, for pharmaceuticals and medical technology;
- NanoFab, for electronics; and
- NanoChance, a BMBF funding measure for targeted support of R&D -intensive small and medium-sized enterprises.

Existing policy actions were re-organised under the umbrella of the **High-Tech Strategy**[581] in 2006. This was done through the **Nano Initiative—Action Plan 2010**[582], a cross-departmental initiative by seven departments of the Federal Government that started in 2007 and was headed by the BMBF. Tying in with BMBF's 2004 Innovation Initiative for Nanotechnology, the action plan aimed to integrate nanotechnology funding in the various policy fields into a national nanotechnology strategy. The Action Plan's main goals were (1) to speed up the use of the results of nanotechnological research for innovations; (2) to introduce nanotechnology to more sectors and companies; (3) to eliminate obstacles to innovation by means of early consultation in all policy areas; and (4) to enable an intensive dialogue with the public. The focus was on the opportunities offered by nanotechnology, but possible risks were also taken into account. The total funding for the years 2007 to 2009 was EUR 640 million.

In 2011, the German Ministry for Education and Research (BMBF) published the **Action Plan Nanotechnology 2015**[583], outlining the strategy for responsible development, innovation and public dialogue for the period 2010-2015. The plan included proposals for developing nanotechnology in five main areas (climate/energy, health/food and agriculture, mobility, communication and security). In parallel, a new funding instrument was launched - **Innovation Alliances** - to provide funding for strategic co-operation between industry and public research in key technology areas that demand a large amount of resources and a long time horizon, but promise considerable innovation and economic impacts. Public funds and funding from the industry is combined in a typical proportion of 1:5 (public: private). Innovation was supported with special emphasis on SMEs and development of value chains. Risk assessment was incorporated as well as an improvement of boundary conditions such as educating the workforce, and addressing issues of legislation, norms and standards. The public dialogue on nanotechnology was intensified, including information and dialogue with citizens as well as stakeholders and NGOs.

Innovation alliances were launched as a successor to the leading edge innovation programmes. They were planned as an instrument of public support to ground-breaking industrial innovation, providing support funding for strategic co-operation between industry and public research in high-potential technology areas that require high levels of funding and long lead times. Through a public-private partnership, the Federal Government provided funding for R&D and other innovation-related activities for specific, long-term co-operative R&D projects. R&D activities could range from fundamental research to prototype development. Public funds were complemented by private money from industry, typically at a proportion of 1:5 (public: private). Each innovation alliance was set up through an industry initiative, organised as a long-term co-operative research project and involving several industry partners as well as public research organisations.

An Innovation Alliance that followed this policy approach was on "Molecular Imaging for Medical Engineering" (nanotechnology) and was formed by Bayer Schering Pharma AG, Boehringer Ingelheim Pharma GmbH & Co. KG, Carl Zeiss AG, Karl Storz & GmbH Co. KG and Siemens AG. The alliance's goal was creating new diagnostic agents and imaging procedures for clinics and the development of pharmaceuticals.

In addition to policies and programmes to support R&D and commercialisation, Germany took action to address concerns about the environmental and safety costs of the nanotechnology. These are particularly important to look at when trying to develop and label commercial nanotechnology products for the market. In response to these issues, governments have increasingly included the concept of responsible development in their nanotechnology activities. Responsible development aims to stimulate the growth of nanotechnology applications in diverse sectors of the economy, while addressing the potential risks and the ethical and societal challenges the technology might raise. Germany has dedicated policies for the responsible development of nanotechnology. The report "Responsible Handling of Nanotechnologies" ("Verantwortlicher Umgang mit Nanotechnologien") launched by the Nano-Commission of the German Federal Government in December 2010 showed

[581] http://www.research-in-germany.org/en/research-landscape/r-and-d-policy-framework/high-tech-strategy.html
[582] http://www.cleaner-production.de/fileadmin/assets/pdfs/Nano_initiative_action_plan_2010.pdf
[583] http://www.lai.fu-berlin.de/homepages/nitsch/publikationen/Germany_ActionPlanNanotechnology_2015.pdf

that the nanotechnology sector is continuing to develop dynamically.

Regional initiatives in Germany that make specific mention of nanotechnology include:

- Innovation Strategy of Nordrhein-Westfalen (2006): This strategy was a government statement dated 26 June 2006. It presented a short analysis of the importance of innovations for North Rhine-Westphalia, and in the following elaborated the overall strategy and the measures employed and purposes targeted. The government strategy aimed to generate new potential for growth by reinforcing strengths, sharpening profiles, promoting excellence and pooling forces. Thus, the funding of research and technology was focused on four priority areas with high potential both related to innovation, employment and growth: (i) *nanotechnology,* microtechnology and new materials; (ii) biotechnology; (iii) energy- and environmental research; and (iv) medical research, medical engineering.
- Cluster Offensive Bayern (2007)[584]: The Bavarian cluster policy was initialised in 2007 and focused on 19 branches/technologies with high importance for the future of Bavaria. These were organised into five fields:
  - materials engineering (including *nanotechnologies*, materials engineering, chemical industries);
  - mobility (including automotive, rail, logistics, aerospace and satellite navigation);
  - life sciences and environment (including biotechnology, medical technologies, energy technologies, environmental technologies, forestry and food);
  - IT and electronics (ICT, high-performance electronics, mechatronics and automation); and
  - service and media (financial services, media).

After a positive evaluation in 2010, the State Government announced some changes in the future organisation of the overall initiative: A major change is that the (nonetheless successful) clusters high-performance electronics, logistics, biotechnology and medical technologies would be restructured into networks, while future funding would be focused on the other clusters, where funding so far was most successful in generating additionality.

- Research Strategy of Thuringia (2008): Main objectives of Thuringia's research policy were to strengthen regional universities and non-university research institutes and regional companies in their research and development efforts in order to achieve scientific excellence, to initiate knowledge and technology transfer as well as innovation. The document described outstanding research areas of the state and measures to strengthen and relate the regional research landscape to target fields in the regional economy: micro and nano technologies, microelectronics; information and communication technologies; media and communication; health research and medical technology; microbiology and biotechnology; optical technologies, photonics; materials and production technologies; environmental and energy technologies, infrastructure; and cultural and social change. Main fields of activity of regional research policy were (i) to support competitiveness, (ii) to strengthen networks, (iii) to support young researchers, and (iv) to invest in infrastructure.

IRELAND

Following the establishment of Science Foundation Ireland (SFI) in 2000, public funding was made available to support many public research initiatives including the **Centre for Research on Adaptive Nanostructures and Nanodevices (CRANN)[585]**. Since its foundation in 2003, CRANN has become a research institute of international standing with 17 Principal Investigators (PIs) across multiple disciplines including physics, chemistry, medicine, engineering and pharmacology, and a total of 250 researchers. CRANN was funded predominately by Science Foundation Ireland (SFI), in partnership with two universities (Trinity College Dublin and University College Cork) and industry, and was formed to harness the cross-disciplinary nanoscience research of individual PIs to deliver world leading research outputs and to enable CRANN researchers to address key industry challenges.

In addition, in December 2009, the **Competence Centre in Applied Nanotechnology (CCAN)** was launched. It was an industry-led, collaborative, applied research centre enabling its member companies and research providers to work together to develop nanotechnology enabled products and solutions for the ICT and biomedical industries (i.e. diagnostics, drug delivery, and regenerative medicine). It was co-hosted by CRANN and Tyndall National Institute at University College Cork. With a growing membership, the founding industry members were Aerogen, Analog Devices, Audit

[584] https://www.cluster-bayern.de/en/
[585] http://www.crann.tcd.ie/

Diagnostics, Creganna-Tactx, Intel, Medtronic, Proxy Biomedical and Seagate. CCAN ran until mid-2015.

Ireland has developed its reputation in nanoscience with its researchers recently ranked sixth globally for the quality of their research. Active collaborations between industry and academia exists and are beginning to deliver significant economic benefits to Ireland. Three of the largest industries in Ireland are directly impacted by nanoscience research in perhaps – medical devices, pharmaceuticals and ICT.

The industry ministry, the Department for Jobs, Enterprise and Innovation (formerly the Department of Enterprise, Trade and Employment) plays a pivotal role in industrial innovation policy with its agencies, Enterprise Ireland (EI) (responsible for supporting Irish companies); Science Foundation Ireland (SFI) (funding basic and applied research); and IDA Ireland (in charge of overseas inward investments).

Apart from the establishment of research infrastructures, policy priorities were also being addressed in the Irish national innovation system. In 2004, the Irish Council for Science, Technology and Innovation, with its Secretariat provided by Forfás, launched **its ICSTI Statement on Nanotechnology**. The Statement assessed Ireland's capabilities in the field of nanotechnology, mapped out specific areas of opportunity for the Irish economy and presented a sustainable vision and strategy for the promotion, development and commercialisation of nanotechnology in Ireland. Among the key application areas that were identified were also pharmaceutical and medical technologies.

In 2010, Forfás[586] itself launched a report on **'Ireland's Nanotechnology Commercialisation Framework 2010 – 2014'**. The report presented a national framework to position Ireland as a knowledge and innovation centre for certain niche areas of nanotechnology. It highlighted that Ireland's nanotechnology players should focus on three main technology areas (advanced materials, "More than Moore" and nanobiotechnology) and four application areas (next generation electronics, medical devices & diagnostics, environmental applications, and industrial process improvements).

The BioNano Laboratory in CRANN (mentioned above) is dedicated to interdisciplinary research at the interface between the physical and life sciences including nanotechnology and diagnostics, nanotoxicology and nanomedicine. The group investigates molecular, cellular and physiological interactions using novel biophysical tools such as cell actuators, and magnetic and ultrasound fields. Members of the BioNano Laboratory are also members of the **Integrated Nanoscience Platform for Ireland (INSPIRE)[587],** a consortium of all Irish third level institutions with international leading research capability in nanoscience and nanotechnology. Furthermore, CRANN is also part of the Molecular Medicine Institute which is a not for profit company established by an extended network of Irish Universities and their associated academic hospitals. The BioNano Laboratory aims to facilitate and accelerate the translation of biomedical nanotechnology research into improved nanoscale diagnostics and nanomedicine.

In October 2013, a new Science Foundation Ireland funded research centre, **Advanced Materials and BioEngineering Research (AMBER)[588]** was launched. AMBER is jointly hosted in TCD by CRANN and the Trinity Centre for BioEngineering, and works in collaboration with the Royal College of Surgeons in Ireland and UCC. The centre provides a partnership between leading researchers in material science and industry to develop new materials and devices for a range of sectors, particularly the ICT, medical devices and industrial technology sectors.

THE NETHERLANDS

In the Netherlands, nanotechnology was established as a distinct field of scientific research in the early years of the 21st century. A foresight study (Ten Wolde 1998) conducted by the Dutch Study Centre for Technology Trends (STT) between 1996 and 1998 laid the foundation of a national research agenda. The study showed the importance of nanotechnology for electronics, materials, molecular engineering and instrumentation, and also recommended to pay due attention to nanosafety issues and set up research in that area.

The Netherlands hosts three dedicated nanotechnology research centres: The University of Twente

[586] Forfás ceased to exist in 2015 and was, in part, subsumed under the Department of Jobs, Enterprise and Innovation.
[587] http://www.crann.tcd.ie/Research/Academic-Partners/testt.aspx
[588] http://ambercentre.ie/

(with the **Mesa+** research centre in microsystems technology and nanomaterials[589]), Delft University of Technology (with the **Else Kooi Laboratory**[590], previously called Dimes research centre on nanoelectronics) and the University of Groningen (with **BioMaDe**[591] focused on bio-nanotechnology). The early 2000s, these formed the core of **NanoNed** - the Nanotechnology R&D initiative in the Netherlands[592]. NanoNed was initiated after three years of preparatory work in 2004 by nine industrial and scientific partners including Philips and TNO. It clustered the Dutch expertise on nanotechnology and enabling technology into a national network. The total budget of the NanoNed programme amounted to EUR 235 million, funded by the Dutch Ministry for Economic Affairs. The NanoNed programme was organised into eleven independent programmes or flagships. Each of those was based on regional R&D strength and industrial relevance. The flagships were Advanced NanoProbing, BioNanoSystems, Bottom-up Nano-Electronics, Chemistry and Physics of Individual Molecules, Nano Electronic Materials, NanoFabrication, Nanofluidics, NanoInstrumentation, NanoPhotonics, Nano-Spintronics and Quantum Computing.

In 2006, the Cabinet vision on Nanotechnology "**From Small to Great**" was published. The content of the document mirrored the outline of the European Commission's 2005 Action Plan, with sections on business and research opportunities; societal, ethical, and legal issues; public engagement; and risk assessment.

In 2008, the Dutch Government published its **Nanotechnology Action Plan**[593]. The plan, prepared by the Interdepartmental Working Grou #p on Nanotechnology (ION) and building on the 2006 vision document, incorporated the most up-to-date scientific findings, and reflected information and agreements from European Union and other international initiatives. Four generic themes were defined on the basis of the central theme impact on society and risk analysis, i.e.: bio-nano-technology, beyond Moore, nanomaterials, and nano production (including instrumentation and characterisation). In addition, four application areas were singled out: clean water, energy, food and "nanomedicine".

The Dutch systematic approach to nanotechnology strategy resulted in the development of stable research groups, centres, department and laboratories. On the national level, **NanoLab NL**[594] formed a consortium that built, maintained and provided a coherent and accessible infrastructure for nanotechnology research. NanoLab drew on government funding, which was first spent on upgrading existing infrastructure. Only when the existing infrastructure was fully used and a well-characterised additional need was identified and additional investment made. As a consequence, the Dutch nanotechnology research infrastructure was heavily used by research groups and the local industry. The partners in this enterprise considered themselves often as competitors but co-operate and co-ordinate their actions because of the substantial government funding.

In 2011, the **NanoNextNL**[595] national research programme on nanotechnology was started as a continuation of NanoNed and MicroNed (the Netherlands Microtechnology program). NanoNextNL is based on a Strategic Research Agenda that was asked for by the government in both the cabinet and the action plan. Risk evaluation and Technology Assessment form part of this research programme. 15% of the budget is dedicated to risk-related research, as was demanded by government in the action plan. It is planned that NanoNextNL programme will finish in 2016 but anticipated that many aspects of it will be continued under an industry umbrella. Since 2011, the research agenda for nanotechnology is also part of the **Top sector policy of the Netherlands**[596], which aims to enhance the knowledge economy by stimulating nine top sectors (leading economic sectors).

The Top sector policy is implemented via innovation contracts, in which agreements are laid down between business leaders, researchers and government, jointly focusing the available resources for knowledge and innovation towards the leading economic sectors. Support programmes that aim to support the development and deployment of nanotechnology, are mostly project based. The formats for such supports range from small business oriented measures to financing large research project which involve co-operation between private and public research performers.

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589 https://www.utwente.nl/mesaplus/
590 http://ekl.tudelft.nl/EKL/Home.php
591 http://www.biomade.nl/
592 However, four other universities, and TNO, the Netherlands Organisation for Applied Scientific Research, are also represented.
593 http://www.rritrends.res-agora.eu/uploads/27/8079721-bijlage%281%29.pdf
594 http://www.nanolabnl.nl/
595 http://www.nanonextnl.nl/
596 http://topsectoren.nl/english

POLAND

In 2000, the Polish State Committee for Scientific Research (KBN) started a targeted research project in the topic of nanotechnology called "**Metallic, Ceramic and Organic Nanomaterials: Processing – Structure – Properties – Applications**" with two aims:

- stimulating research on nanomaterials in Poland and promoting collaboration between researchers in this field; and
- making a landscape of the status of nanotechnology in Poland.

The project involved 15 scientific institutions working on 26 research tasks.

In the Polish National Development Plan for the years 2007-2013, launched by the State Committee for Scientific Research in Warsaw in 2004, nanotechnology was foreseen as an area that should contribute to achieving a significant competitive potential in the European Arena.

During 2006, the Ministry of Science of Higher Education established the Interdisciplinary Committee for Nanoscience and Nanotechnology. This Committee analysed the nanotechnology situation and capabilities in Poland and proposed the basic fields that should be strategically supported and launched in 2007 the "**Strategy for the Reinforcement of Polish Research and Development Area in the Field of Nanosciences and Nanotechnologies**"[597]. The areas to be supported were nanoscale phenomena and processes, nanostructures, nanomaterials and nanoscale devices on the one side and nano-analytics/nano-metrology and manufacturing processes and devices for nanotechnology on the other. The priority of the strategy of nanosciences and nanotechnologies was the development, co-ordination and management of the national system of research, education and industry in this field in the short-, medium-, and long-term perspective. Other main objectives to be achieved by 2013 were the development of high added-value nanotechnology products, the creation and commercialisation of manufacturing devices for the production of nanomaterials, the development of the education system in the field of nanotechnology, educating about 20-30 doctors yearly in the specialisation of nanotechnology, building specialist laboratories, establishing co-operation networks of research and industrial units, financial institutions, etc. and integrating dispersed activity of research units in a joint programme of nanotechnology development.

In 2014, the Government approved the **National Smart Specialisation Strategy** as an integral part of the Enterprise development Programme, setting "Multifunctional materials and composites with advanced properties, including nano-processes and nano-products" as a horizontal smart specialisation area in Poland.

PORTUGAL

In 2005, the Portuguese and Spanish Governments decided to jointly create the **International Nanotechnology Laboratory (INL)**[598] in Braga, Portugal, which was partly funded under the European Regional Development Fund (ERDF). The decision of Portugal and Spain to create an international research laboratory was announced by the head of Government of Spain and the Prime Minister of Portugal at the end of the XXI Portugal-Spain Summit that took place in Évora, Portugal.

The International Nanotechnology Laboratory (INL) was installed in Braga, Portugal, its Director is the Swedish Professor Lars Montelius, and it has over 90 employees.

INL concentrates on nanotechnology, and considers applications to several other areas, following a truly interdisciplinary approach. The Laboratory has been conceived to:

- Assure world class research excellence in all areas of activity;
- Develop partnerships with the industry and foster the transfer of knowledge in economic values and jobs;
- Train researchers and contribute to the development of a skilled workforce for the nanotechnology industry; and
- Survey, prevent and mitigate nanotechnology risks.

Among its research areas nanomedicine, nano-electronics, nano-machines & nano-manipulation and environment monitoring, security and food quality control can be found.

Further information on the policies and programmes of Spain is given below.

[597] www.bioin.or.kr/fileDown.do?seq=5186
[598] http://inl.int/

SPAIN

The Minister of Economy and Competitiveness is responsible for the design of the national innovation strategy in Spain. An Inter-Ministerial Commission on Science and Technology (CICYT) has the role of co-ordinating the actions of the different bodies involved in innovation policy in a complex governance structure. The regions of Catalonia, the Basque Country and Valencia are especially active in S&T policy.

The 2004-2007 R&D plan was the first Spanish national R&D plan containing a specific cross-programme action regarding nanoscience and nanotechnology. The **Strategic Action (SANSNT)** was designed for the overall enhancement of Spanish industry competitiveness through the implementation of deep changes in several industrial sectors by generating new knowledge and applications based on the convergence of new technologies, where nanotechnology plays a central role. The SANSNT included seven thematic lines among which the first one is "***Nanotechnologies*** applied in materials and new materials within the field of health". Also included are systems biology, synthetic biology and *nanobiotechnology*. The Strategic Action encompassed the development of activities within the six Instrumental Lines of Action (human resources; projects; institutional strengthening; infrastructures; knowledge use; and articulation and internationalisation of the system).

Nanoscience and nanotechnology were included as a **Strategic Action** of both the 2004-2007 National Plan for Research, Development and Innovation (R+D+I) and the funding set aside within this Plan for the Industrial Sector (PROFIT Programme), with the aim of promoting the development of industrial projects (carried out by companies) with nanotechnology-focused objectives.

During the 2004-2007 periods, around 40 projects were funded as a result of this Strategic Action, receiving a total of EUR 2 million in subsidies and EUR 8.5 million in associated investments. All the projects were coordinated by industrial companies, although universities and technological centres were involved in the development of many of them either on a collaborative basis, or were subcontracted by the company carrying out the project.

In 2005, the Government of Spain launched the strategic programme **INGENIO 2010**[599] to align Spain with the strategy of the European Union to reach a 3% of the GDP invested in R&D by year 2010, thereby reducing the gap between Spain and other countries. Its general objective was to achieve a gradual focus of Spanish resources on strategic actions to meet the challenges faced by the Spanish Science and Technology System. This was to be achieved by continuing the existing policies, agendas and successful programmes, as well as by implementing new actions needed to finish meeting the challenges identified for the national science, technology and engineering system.

In order to enhance critical mass and research excellence, the goals of the INGENIO 2010 Programme, within the **CONSOLIDER programme** (launched by the Ministry of Education and Science, through the General Secretariat of Scientific Policy, to promote high quality research and to reach critical mass and research excellence), included creating Centros de Investigación Biomédica en Red (Biomedical Research Networking Centres, CIBER) by setting up consortia, with their own legal personality, without physical proximity, which were designed to conduct single-topic research on a specific broadly-defined disease or health problem. CIBER were formed through the association of research groups linked to the national health system to help form the scientific basis of the programmes and policies of the national health system in the priorities areas of the National R+D+I Plan. Among the centres that have been created within this programme is the Biomedical Research Networking centre in Bioengineering, Biomaterials and ***Nanomedicine*** (CIBER-BBN), founded in 2006. The ***Nanobiomed consortium***, which researches the use of nanoparticles for drug delivery, was also founded with CONSOLIDER funds.

Between 2008 and 2011 the **National Strategy of Nanoscience and nanotechnology, new materials and new industrial products**[600] was implemented by the Ministry of Economy and Competitiveness. This policy measure was part of the National Plan for R+D+I 2008-2011[601] and its objective was to enhance the competitiveness of Spanish industry by promoting knowledge about and stimulating the development of new applications based on nanoscience, nanotechnology, material science and technology, and process technologies. Six themes were targeted: Nanotechnologies applied to materials and new materials in health sector, nanotechnologies for information and telecommunications, nanotechnologies in relation to industry and climate, smart

[599] http://www.ingenio2010.es/
[600] http://www.idi.mineco.gob.es
[601] Ibid

materials with tailored properties based on knowledge as materials and performance coatings for new products and processes, advances in technology and materials processing, development and validation of new industrial models and strategies/new technologies for manufacturing design and process/network production, and exploitation of convergent technologies. The measure covered different lines such as supporting investments, projects, institutional strengthening, infrastructure and utilisation of knowledge, supporting first market operations for innovative products and access to early stage/development funding, system articulation and internationalisation and targeted public research organisations, SMEs and other companies.

Both in the last Spanish Strategy of Science, Technology and Innovation 2013-2020[602] and in the State Plan of Scientific and Technical Research and Innovation 2013-2016[603] (both dependent on the Ministry of Economy and Competitiveness), nanotechnology is considered a sector to be boosted when referring to Key Enabling Technologies (KETs), but there is not a strategic plan such as in previous periods.

Regional initiatives in Spain include:

- Estrategia Nanobasque (2008)[604]: In order to promote the implementation of micro and nanotechnologies in the Basque companies, the Basque Government designed a strategy called NanoBasque in 2007. On December 3 2008, the Department of Industry, Trade and Tourism of the Basque Government launched the nanoBasque Strategy in the framework of the Basque Science, Technology and Innovation Plan 2010. The nanoBasque Strategy was an initiative designed to develop a new economy sector enabled by nanotechnology. It was created with the purpose of covering three main areas of action, namely: company, knowledge and society. One of the objectives was to create a new model of relations to involve both national and international companies, scientific, technological, political and social agent. The expected result were targeting the efficiency and the integration of the ecosystem of innovation that was clearly aimed at the market, based on the co-operation between all parties. The launch of the nanoBasque Strategy was accompanied by the creation of a dynamic support agency, the nanoBasque Agency, with the mission of coordinating and managing the development of the Strategy. The nanoBasque Strategy strived to boost Basque the presence of companies and research agents on international nanotechnology initiatives and markets. EUR 550 million were expected to be mobilised in the 2009-2015 period, with a proportion of public funding of 52% on the total.
- Within the nanoBasque strategy and using CONSOLIDER funds, the Cooperative Research Center NanoGUNE was created with the mission of performing world-class nanoscience research for the competitive growth of the Basque Country, thereby combining basic research with the objective of boosting nanotechnology-based market opportunities and contributing to the creation of an enabling framework to remove existing barriers between the academic and business worlds.
- The Andalusian Centre for Nanomedicine and Biotechnology, BIONAND, is a mixed centre part owned by the Regional Ministry of Health and Social Welfare, the Regional Ministry of Finance, Innovation, Science and Employment and the University of Malaga. BIONAND has been co-financed, with a contribution of 70% of the total cost, by the European Regional Development Fund (ERDF) together with the Ministry of Economy and Competitiveness in the frame of The Spanish National Plan for Scientific Research, Development and Technological Innovation 2008-2011 (record number, IMBS10-1C-247, quantity. EUR 4.9m). The three main research areas are nanodiagnostics, therapeutic nanosystems, and nanobiotechnology.
- IMDEA-Nanociencia is a private non-profit Foundation created by the regional Government of the Community of Madrid in November 2006 to shorten the distance between the research and society in the Madrid region and provide new capacity for research, technological development and innovation in the field of nanoscience, nanotechnology and molecular design. Researchers at IMDEA Nanoscience are developing distinct diagnostic tools, including nucleic acid-based and nanoparticle-based sensors for detection of biological targets of medical interest, and magnetic nanoparticles to be used in medical imaging as high-sensitive contrast agents.

[602] http://www.idi.mineco.gob.es/stfls/MICINN/Investigacion/FICHEROS/Spanish_Strategy_Science_Technology.pdf
[603] http://www.idi.mineco.gob.es/stfls/MICINN/Investigacion/FICHEROS/Spanish_RDTI_Plan_2013-2016.pdf
[604] http://www.nanobasque.eu/aNBW/web/en/strategy/index.jsp

THE UNITED KINGDOM (UK)

The main player in UK policy measures related to nanotechnology as a key enabling technology (KET) is the Department for Business, Innovation and Skills (BIS) and its agency, the Technology Strategy Board, now called Innovate UK[605]. It supports SMEs with high growth potential, manages the Small Business Research Initiative[606] and identified future potential growth sectors. Both institutions have also developed a number of measures facilitating the knowledge exchange and technology adoption, such as: commercialisation opportunities and Knowledge Transfer Partnerships, Knowledge Transfer Networks, Technology and Innovation Centres, and Small Businesses Research Initiative.

The main interest of the UK government for nanotechnology started in 2002, when they published the **Taylor Report**[607] which recognised that investment in nanotechnology was increasing rapidly worldwide. Following the Taylor Report, an announcement was made by Lord Sainsbury of GBP 90m of funding for the Micro and Nano Technology Manufacturing Initiative. This funding was committed between 2003 and 2007. **Micro- and Nano-technology Manufacturing Initiative** (MNT Initiative) were joint investments by the Government, the Regional Development Agencies (RDAs) and the devolved administrations of Wales and Scotland. The Initiative was launched to help the industry build on the expertise of the UK science base and win a share of this developing market, harnessing the commercial opportunities offered by nanotechnology.

Approximately one third of this investment went to Collaborative R&D MNT Projects, and two thirds to capital infrastructure. Generally built on existing university or business expertise, the twenty-four facilities were targeted at addressing a broad range of key application areas where micro/nano scale activity was considered key to future UK industry capability and where the UK had some strength. Micro/nano technologies were included within relevant broader collaborative R&D competitions, principally in the materials, medicine and electronics areas. In 2007 the **Nanotechnology Knowledge Transfer Network (NanoKTN)[608]** was created with the objective of supporting the exploitation and commercialisation of MNT through informing, linking and facilitating innovation and collaborations between users and suppliers of nanotechnology in order to build a strong MNT community in the UK. The centres were grouped into four main themes: nano-metrology; nanomaterials (including health and safety); nanomedicine; and nanofabrication. Between its creation and 2014 the NanoKTN secured about £82million for UK industry, mainly focussed on SMEs, providing a good return investment on the initial input of £3million. In 2014, NanoKTN was merged with another 15 KTN in the new organisation KTN Ltd.

In 2006, the Engineering and Physical Sciences Research Council issued its **Report of the Nanotechnology Strategy Group[609]** as an active response to the EPSRC 2005 Nanotechnology Theme Day Report that found that there were flaws in the structure for nanotechnology R&D in the UK. The report proposed, in conjunction with researchers and users, to identify a series of "grand challenges" in nano-science and nano-engineering, focused initially on areas such as energy, environmental remediation, the digital economy and healthcare, where an interdisciplinary, stage-gate approach spanning basic research through to application will be an integral part of the challenge of enabling nanotechnology to make an impact. The "grand challenges" were to be addressed via interdisciplinary consortia spanning the EPSRC research spectrum, and including collaboration with sister Research Councils (e.g. BBSRC).

In December 2007, the Research Councils announced a Cross-Council programme "**Nanoscience through Engineering to Application[610]**", with the objective of providing an additional GBP 50 million in areas where the UK nanotechnology research base could make a significant impact on issues of societal importance such as healthcare. These societal or economic Grand Challenges wanted to be addressed in a series of calls for large-scale integrated projects. They were led by the Engineering and Physical Sciences Research Council, in collaboration with stakeholders including other Research Councils, industry, the Technology Strategy Board (TSB) and the Nanotechnology Research Coordination Group.

Government announced its intention to develop a UK Strategy for nanotechnologies in its 2009 response to the Royal Commission on Environmental Pollution's report, Novel materials in the

[605] https://www.gov.uk/government/organisations/innovate-uk
[606] https://www.gov.uk/government/collections/sbri-the-small-business-research-initiative
[607] http://webarchive.nationalarchives.gov.uk/20130221185318/http://www.innovateuk.org/_assets/pdf/taylor%20report.pdf
[608] https://connect.innovateuk.org/web/nanoktn
[609] https://www.epsrc.ac.uk/newsevents/pubs/report-of-the-nanotechnology-strategy-group/
[610] https://www.epsrc.ac.uk/newsevents/pubs/nanotechnology-programme/

Environment: The case of Nanotechnology.

The **Nanoscale Technologies Strategy 2009-2012**[611] was launched in October 2009 by the TSB and targeted the ways by which nanotechnologies could address major challenges facing society such as environmental change, ageing and growing populations, and global means of communication and information sharing. Its objective was to provide the framework for future applied research predominantly through activity inspired by the needs of wider technologies and challenge-led calls.

In 2010, the Ministerial Group on Nanotechnologies, the Nanotechnology Research Co-ordination Group (NRCG), and the Nanotechnology Issues Dialogue Group (NIDG) issued the UK **Nanotechnologies Strategy - Small Technologies, Great Opportunities**[612]. This Strategy defined how Government will take action to ensure that everyone in the UK could safely benefit from the societal and economic opportunities that these technologies offer, whilst addressing the challenges that they might present.

In 2012 the Department for Environment, Food and Rural Affairs (DEFRA) launched the **Nanotechnology Strategy Forum (NSF)**[613] to facilitate discussion and engagement between Government and stakeholders in matters referred to the responsible advancement of the UK's nanotechnologies industries. The NSF is an advisory body formed by *ad hoc* expert with a membership drawn from industry, regulators, academia and NGOs (non-governmental organisations and it is jointly chaired by the Minister of State for Universities and Science (BIS) and the Parliamentary Under-Secretary for DEFRA and is supported by a small secretariat based in DEFRA.

The UK **Enabling Technologies Strategy 2012-2015**[614] also addresses four enabling technologies - advanced materials; biosciences; electronics, sensors and photonics; and information and communication technology (ICT) to support business in developing high-value products and services in areas such as energy, food, healthcare, transport and the built environment. Nanotechnology is identified as having a significant underpinning role across most of these technology areas, particularly in the healthcare and life sciences sectors.

[611] http://www.nibec.ulster.ac.uk/uploads/documents/nanoscaletechnologiesstrategy.pdf
[612] http://www.steptoe.com/assets/htmldocuments/UK_Nanotechnologies%20Strategy_Small%20Technologies%20Great%20Opportunities_March%202010.pdf
[613] https://www.gov.uk/government/groups/nanotechnology-strategy-forum
[614] https://www.gov.uk/government/publications/enabling-technologies-strategy-2012-to-2015

ANNEX 7: ADDITIONAL PATENT DATA

This section provides the following tables:

- Number of patent families for top 25 universities and public research organisations (1993-2011)
- Universities / research organisations granted patents, by EPO patent numbers (1993-2011)
- Number of patent families for top ten universities and public research organisations (1993-2011)
- Companies with the highest number of patent families (percentage of patent families including PCT, US and EP applications)

Table A1: Number of patent families for top 25 universities and public research organisations (1993-2011)

	Country	Organisation	No. of Patent families	PCT	US	EP
1	United States	University of California	58	63.8%	79.3%	32.8%
2	United States	MIT	41	82.9%	75.6%	39.0%
3	United States	University of Texas	22	4.5%	81.8%	40.9%
4	United States	Northwestern University	18	72.2%	77.8%	11.1%
5	United States	University of Michigan	18	50.0%	72.2%	38.9%
6	United States	Johns Hopkins University	16	37.5%	75.0%	37.5%
7	United States	Emory University	16	87.5%	68.8%	50.0%
8	United States	Rice University	14	78.6%	50.0%	14.3%
9	United States	General Hospital Corp	14	85.7%	64.3%	21.4%
10	France	CNRS	14	64.3%	57.1%	64.3%
11	United States	Brigham & Women's Hospital	12	66.7%	75.0%	16.7%
12	United States	University of North Carolina at Chapel Hill	11	63.6%	63.6%	36.4%
13	United States	Research Foundation of State University of New York	11	72.7%	36.4%	36.4%
14	United States	Stanford	10	30.0%	80.0%	30.0%
15	United States	Harvard College	10	70.0%	60.0%	20.0%
16	United States	California Inst. of Tech.	10	80.0%	80.0%	60.0%
17	Japan	JP S&T Agency[615]	19	68.4%	31.6%	42.1%
18	Brazil	Uni. Fed. Minas Gerais	9	66.7%	0.0%	22.2%
19	Singapore	Agency for Science Tech & Research	9	66.7%	44.4%	44.4%
20	Israel	Ramot at Tel Aviv University Ltd	8	75.0%	75.0%	50.0%
21	Israel	Technion R&D Foundation Ltd	8	25.0%	100.0%	25.0%
22	United States	University of Washington	8	50.0%	75.0%	12.5%
23	United States	University of Florida Research Foundation	8	50.0%	87.5%	62.5%
24	United States	Scripps Research Institute	8	87.5%	75.0%	75.0%
25	Korea (South)	KIST	7	14.3%	57.1%	0%

[615] The Japanese S&T Agency (JST) was formed in October 2003 as a successor of the Japanese S&T Corporation which was itself a merger in 1996 of the Japan Information Centre of Science and Technology (JICST founded 1957) and the Research Development Corporation of Japan (JRDC, founded 1961). These figures incorporate data for both the JST Agency and the JST Corporation. http://erawatch.jrc.ec.europa.eu/erawatch/opencms/information/country_pages/jp/organisation/organisation_mig_0008

Table A2: Universities / research organisations granted patents, by EPO patent numbers

Rank	Country	Organisation	EP	US
1	US	University of California	3	18
2	US	Scripps Research Institute	3	4
3	**FR**	CNRS	3	4
4	US	University of Louisville Research Foundation Inc	3	3
5	**ES**	Consejo Superior De Investigaciones Cientificas	3	1
6	US	MIT	2	15
7	JP	Japanese S&T Agency	2	3
8	US	Johns Hopkins University	2	3
9	**CH**	ETH Zurich	2	2
10	IN	Council of Scientific & Industrial Research	2	1
11	US	Mayo Foundation	2	1
12	UK	University of Strathclyde	2	1
13	**IT**	Universita Degli Studi di Roma La Sapienza	2	0
14	**UK**	University of Glasgow	2	0
15	US	University of Texas System	1	7
16	US	University of Michigan	1	7
17	US	Stanford Junior University	1	6
18	US	California Institute of Tech	1	5
19	US	Emory University	1	5
20	US	Northwestern University	1	5
21	US	University of Illinois	1	5
22	US	University of Florida Research Foundation Inc.	1	5
23	**ES**	Universidad De Sevilla	1	5
24	US	New York University	1	4
25	US	University of Washington	1	4

Table A3: Number of patent families for top ten universities and public research organisations (1993-2011)

Rank	Country	Organisation	EP	US
1	US	University of California	3	18
2	US	MIT	2	15
3	US	University of Texas System	1	7
4	US	University of Michigan	1	7
5	US	Stanford University	1	6
6	US	California Institute of Technology	1	5
7	US	Emory University	1	5
8	US	Northwestern University	1	5
9	US	University of Illinois	1	5
10	US	University of Florida Research Foundation Inc.	1	5
11	ES	Universidad de Sevilla	1	5
12	TN	Industrial Tech Research Institute	0	5
13	US	Scripps Research Institute	3	4
14	**FR**	CNRS	3	4
15	US	New York University	1	4
16	US	University of Washington	1	4
17	US	University of Michigan	0	4
18	US	University of Louisville Research Foundation Inc.	3	3
19	JP	Japanese S&T Agency	2	3
20	US	Johns Hopkins University	2	3
21	IL	Ramot at Tel Aviv University Ltd	1	3
22	US	Duke University	1	3
23	US	Harvard College	1	3
24	US	University of South Florida	1	3
25	US	John Wayne Cancer Institute	0	3

Table A4: Companies with the highest number of patent families (percentage of patent families including PCT, US and EP applications)

	Country	Company	No. of Patent Families	PCT	US	EP
1	United States	Immunomedics Inc	50	32	44	30
2	United States	IBC Pharmaceuticals Inc	20	4	19	4
3	Netherlands	Kon Philips Elects NV	20	18	12	18
4	France	L Oreal	16	2	5	16
5	United States	Nanosystems Llc	16	14	4	3
6	United States	Neorx Corp	12	11	5	6
7	Barbados	Boston Scientific Ltd	11	4	x	11
8	United States	Boston Scientific Scimed.	11	7	8	3
9	Germany	Schering AG	11	10	4	8
10	United States	Pfizer Inc	10	5	6	5
11	Netherlands	Farmarc Nl Bv	10	6	4	6
12	Ireland	Elan Pharma Int Ltd	9	2	3	9
13	United States	Nanoset Llc	9	9	3	1
14	United States	Procter & Gamble Co	8	8	7	4
15	United States	Abraxis Bioscience Llc	8	1	5	5
16	United States	Cerulean Pharma Inc	8	4	6	1
17	Germany	Siemens AG	8	1	1	1
18	France	Guerbet	8	8	4	7
19	Germany	Philips IP & Standards	8	8		8
20	Germany	Bayer Schering Pharma	7	4	2	4
21	United States	Selecta Biosciences Inc	7	5	7	2
22	Germany	Hexal AG	7	5	2	7
23	Switzerland	Novartis AG	7	2	4	4
24	Japan	Ono Pharma Co Ltd	7	5	5	6
25	United States	Nano Systems LLC	7		7	

ANNEX 8: PRODUCTS FOR NANOTECHNOLOGY AND HEALTH

This Annex is divided into the same categories as used in the main body of the report:

1. Drug delivery vehicles;
2. Biomedical markers and detection aids;
3. Ferrofluids;
4. MRI contrast agents;
5. Surface disinfectants;
6. Proteomics applications;
7. Synthetic bone and tooth enamel;
8. Transfection reagents;
9. Nano-porous membranes;
10. Antimicrobials;
11. Drug production and mixing systems; and
12. Other.

1 DRUG DELIVERY VEHICLES

Product Name	Description	Producer	Sub-sector
Tricor	Fenofibrate as Nanocrystals	Abbott Laboratories	CV
Survanta	Survanta is indicated for treatment of Respiratory Distress Syndrome (RDS) (hyaline membrane disease) in new born premature infants with a birth weight of 700g or greater and who are intubated and are receiving mechanical ventilation. Survanta is also indicated for the prophylactic treatment of premature infants <32 weeks gestational age at risk of developing RDS.	Abbvie Inc.	OTH
Mugard	MuGard® Oral Mucoadhesive is indicated for the management of oral mucositis/stomatitis (that may be caused by radiotherapy and/or chemotherapy) and all types of oral wounds (mouth sores and injuries), including aphthous ulcers/canker sores and traumatic ulcers, such as those caused by oral surgery or ill-fitting dentures or braces.	Abeona Therapeutics/ AMAG Pharmaceuticals	CT
Zanaflex	Zanaflex is a short-acting muscle relaxer. It works by blocking nerve impulses (pain sensations) that are sent to your brain. Zanaflex is used to treat spasticity by temporarily relaxing muscle tone.	Acorda Therapeutics, Inc.	OTH
Verelan/Verelan PM	Verelan is used with or without other medications to treat high blood pressure (hypertension). Lowering high blood pressure helps prevent strokes, heart attacks, and kidney problems. Verapamil is called a calcium channel blocker. It works by relaxing blood vessels so blood can flow more easily. It may also lower the heart rate.	Alkermes Pharma Ireland Ltd	CV
Naprelan	NAPRELAN® may be used to treat rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, tendinitis,	Almatica Pharma, Inc.	OTH

Product Name	Description	Producer	Sub-sector
	bursitis, and acute gout. It may also be used to relieve mild to moderate pain and the treatment of primary dysmenorrhea (menstrual cramps).		
Indaflex	Indaflex is a crème that is used to treat osteoarthritis	AlphaRx	OTH
Neulasta	Neulasta (pegfilgrastim) is a man-made form of a protein that stimulates the growth of white blood cells in your body. White blood cells help your body fight against infection. Neulasta is used to prevent neutropenia, a lack of certain white blood cells caused by receiving chemotherapy.	Amgen Inc.	CT
Zinostatin Stimalamer	Polymer-protein conjugate (Styrene maleic anhydride-neocarzinostatin) to treat hepatocellular carcinoma	Astellas Pharma	CT
Diprivan	Diprivan (propofol) is an injectable general anaesthetic for the induction and maintenance of anaesthesia. It can also be used for sedation of ventilated patients and those undergoing diagnostic or surgical procedures.	AstraZeneca	OTH
Epaxel	Epaxal is a virosomal vaccine to prevent hepatitis A infection	Berna Biotech	ID
Elestrin	This medication is a female hormone (estrogen). It is absorbed through the skin and enters the bloodstream. It is used by women to help reduce a certain symptom of menopause (hot flushes).	BioSante	OTH
Elozyl	Elozyl is dental gel that is being used to treat parodontitis	Camurus	ID
Abraxane	Abraxane is indicated for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within six months of adjuvant chemotherapy.	Celgene	CT
Opaxio	Opaxio™ (paclitaxel poliglumex) is an investigational, biologically-enhanced chemotherapeutic that links paclitaxel, the active ingredient in Taxol®, to a biodegradable polyglutamate polymer, which results in a new chemical entity. When bound to the polymer, paclitaxel is inactive, potentially sparing normal tissue's exposure to high levels of paclitaxel and its associated toxicities. Blood vessels in tumor tissue, unlike blood vessels in normal tissue, are porous to macromolecules such as Opaxio.	Cell Therapeutics, Inc.	CT
Curosurf	Curosurf is used to treat neo-natal respiratory distress	Chiesi Framaceutici SpA	OTH

Product Name	Description	Producer	Sub-sector
Inflexal V	Inflexal V is a virosomal adjuvanted Influenza vaccine (subunit), based upon the virosome technology developed and patented by the Crucell company, Berna Biotech AG. It is the only adjuvanted flu vaccine licensed for all age groups (from 6 months and up).	Crucell NV	ID
Ontak	Denileukin diftitox is used to treat patients with persistent or recurrent cutaneous T-cell lymphoma. The patient's lymphoma cells need to be a specific type -- they must have the high affinity component of the IL-2 receptor -- to be treated with this drug. This is generally confirmed by testing the lymphoma tissue before the drug is given.	Eisai	CT
Rexin-G	Approved for (i) Pancreatic cancer, (ii) Soft Tissue Sarcoma, and (iii) Osteosarcoma. Rexin-G has recently been approved in the Philippines for the treatment of all solid tumors that are refractory to standard chemotherapy.	Epeius Biotechnologies	CT
Kadcyla	KADCYLA® is approved to treat HER2-positive breast cancer that has spread to other parts of the body (metastatic breast cancer) after prior treatment with trastuzumab (Herceptin) and a taxane. Prior treatment could have been for the initial treatment of breast cancer or for the treatment of cancer that had spread to other parts of the body.	F. Hoffmann-La Roche AG	CT
Pegasys	Pegasys (peginterferon alfa-2a) is made from human proteins that help the body fight viral infections. Pegasys is used to treat chronic hepatitis B or C in adults, and to treat chronic hepatitis C in children (5 years and over). It is often used together with another medication called ribavirin (Copegus, RibaPak, Ribasphere, RibaTab).	F. Hoffmann-La Roche AG	ID
Nanoxel	NANOXEL is indicated for the adjuvant treatment of node-positive breast cancer administered sequentially to standard doxorubicin-containing combination chemotherapy.	Fresenius Kabi	CT
DaunoXome	DaunoXome contains an aqueous solution of the citrate salt of daunorubicin encapsulated within lipid vesicles (liposomes) composed of a lipid bilayer of distearoylphosphatidylcholine and cholesterol (2:1 molar ratio), with a mean diametre of about 45 nm.	Galen	CT
AmBisome	AmBisome is used to treat serious, life-threatening fungal infections	Gilead	ID

Product Name	Description	Producer	Sub-sector
	including leishmaniasis, and a certain form of meningitis in people infected with HIV (human immunodeficiency virus).		
Mircera	Mircera is used to treat anemia (a lack of red blood cells in the body) in people with chronic kidney disease. Mircera is not for treating anemia caused by cancer chemotherapy or as a substitute for blood transfusions in patients who require immediate correction of anemia.	F. Hoffmann-La Roche AG	OTH
Invega Sustenna	INVEGA SUSTENNA® (paliperidone palmitate) is indicated for schizophrenia and schizoaffective disorder.	Johnson & Johnson (subsidiary Janssen Pharmaceuticals)	OTH
Amphotec	Amphotec is indicated for the treatment of invasive aspergillosis in patients where renal impairment or unacceptable toxicity precludes the use of conventional amphotericin B in effective doses and in patients where prior amphotericin B treatment has failed.	Marketed by SEQUUS Pharmaceuticals Inc. (Johnson & Johnson), manufactured by Ben Venue Laboratories	ID
Oncaspar	Oncaspar® is indicated as a component of antineoplastic combination therapy for reinduction in acute lymphatic leukaemia (ALL) in children and adults in patients with known hypersensitivity to "native" L-asparaginases.	Medac GmbH	CT
Eligard	Eligard® is a hormone compound for the treatment of advanced, hormone- dependent prostate cancer. The active ingredient (leuprolide acetate) significantly reduces the level of the male sex hormone testosterone, thus suppressing testosterone-dependent tumor growth. The established active ingredient is combined with a novel drug delivery system known as Atrigel® depot technology. The liquid drug is injected subcutaneously and Eligard® forms a gel-like implant which slowly disintegrates, steadily releasing the drug over a period of one, three or six months, depending on the dosage administered.	Medigene AG	CT
Salium	Salium is an oral liquid used to treat Xerostomia	Menarini	OTH
Emend	Emend (aprepitant) blocks the actions of chemicals in the body that trigger nausea and vomiting. Emend is used together with other medications to prevent nausea and vomiting that may be caused by surgery or cancer chemotherapy.	Merck	OTH

Product Name	Description	Producer	Sub-sector
PegIntron®	PegIntron® (Peginterferon alfa-2b) is made from human proteins that help the body fight viral infections. PegIntron®is used to treat chronic hepatitis C in adults. PegIntron® is often used in combination with another medication called ribavirin (Rebetol, Ribasphere) to treat hepatitis C in adults and children who are at least 3 years old.	Merck Sharp & Dohme Corp.	ID
Somavert	SOMAVERT® (pegvisomant for injection) is a prescription medicine for acromegaly. It is for patients whose disease has not been controlled by surgery or radiation, or patients for whom these options are not appropriate. The goal of treatment with SOMAVERT is to have a normal IGF-I level in the blood.	Nektar Therapeutics (in partnership with Pfizer)	OTH
Focalin XR	Dexmethylphenidate is a mild stimulant to the central nervous system. It affects chemicals in the brain that contribute to hyperactivity and impulse control. Dexmethylphenidate is used to treat attention deficit hyperactivity disorder (ADHD).	Novartis	OTH
Ritalin LA	Methylphenidate is a central nervous system stimulant. It affects chemicals in the brain and nerves that contribute to hyperactivity and impulse control. Methylphenidate is used to treat attention deficit disorder (ADD), attention deficit hyperactivity disorder (ADHD), and narcolepsy.	Novartis	OTH
Estraorb	Estradiol gel used to treat menopausal symptoms	Novavax/ Graceway	OTH
Macugen	Pegaptanib sodium injection (brand name Macugen) is an anti-angiogenic medicine for the treatment of neovascular (wet) age-related macular degeneration (AMD).	OSI Pharmaceuticals Inc.	OTH
DepoCyt(e)®	DepoCyt(e)® (cytarabine liposome injection) is a sustained-release liposomal formulation of the chemotherapeutic agent cytarabine utilising Pacira's DepoFoam® technology. DepoCyt(e) is indicated for the intrathecal treatment of lymphomatous meningitis, a life-threatening complication of lymphoma, a cancer of the immune system.	Pacira Pharmaceuticals	ID
Megace ES	Megace (megestrol) is a man-made chemical similar to the female hormone progesterone. Megestrol is used in the treatment of advanced breast cancer and endometrial cancer.	Par Pharma	CT

Product Name	Description	Producer	Sub-sector
Avinza	Avinza (morphine) is an opioid pain medication. An opioid is sometimes called a narcotic. Avinza is used to treat moderate to severe pain caused by cancer.	Pfizer	OTH
Rapamune	Used for prophylaxis of Organ Rejection in Renal Transplantation Rapamune (sirolimus) is indicated for the prophylaxis of organ rejection in patients aged 13 years or older receiving renal transplants.	Pfizer	OTH
Visudyne	Visudyne (verteporfin) is a sterile powder for intravenous infusion. Visudyne therapy is a two-stage process requiring administration of both verteporfin for injection and nonthermal red light. Verteporfin is used as a light-activated drug (photosensitiser). Treatment of diseases using photosensitisers and light activation is called photodynamic therapy (PDT).	QLT / Novartis	OTH
Genexol-PM®	Polymeric micelles based formulation of Paclitaxel (cancer thermotherapy)	Samyang	CT
Renagel	Renagel® is a phosphate binder indicated for the control of serum phosphorus in patients with chronic kidney disease on dialysis.	Sanofi	OTH
Caelyx®	Liposome based formulation of Doxorubicin against Ovarian cancer, Kaposi's sarcoma and breast cancer	Schering (Merck & Co.)	CT
Doxil®	Liposome based formulation of Doxorubicin against Ovarian cancer, Kaposi's sarcoma and breast cancer	Schering Plough	CT
Gendicine	Gendicine is a recombinant adenovirus engineered to express wildtype-p53 (rAd-p53). This virus is designed to treat patients with tumors which have mutated p53 genes.	Shenzhen SiBiono GeneTech	CT
Triglide	Fenofibrate as Nanocrystals	Shionogi Pharma Inc.	CV
Fosrenol	To reduce serum phosphate in patients with end-stage renal disease (ESRD)	Shire	OTH
Adagen	ADAGEN® (pegademase bovine) Injection is a modified enzyme used for enzyme replacement therapy for the treatment of severe combined immunodeficiency (also known as SCID or the "Bubble Boy Disease"), which is caused by the chronic deficiency of the adenosine deaminase (ADA) enzyme.	Sigma-Tau	OTH
Abelcete®	ABELCET® (amphotericin B lipid complex injection) is indicated for the treatment of invasive fungal infections in patients who cannot tolerate, or have failed with,	Sigma-Tau Pharmaceuticals, Inc.	ID

Product Name	Description	Producer	Sub-sector
	conventional amphotericin B therapy.		
episil	episil® is a fast-acting treatment that reduces the pain associated with oral mucositis (OM).	Sinclair/Teva	OTH
Depodur	DepoDur(TM) is a single dose extended-release injectable formulation of morphine sulphate. DepoDur(TM) employs SkyePharma's proprietary DepoFoam(TM)	SkyePharma PLC and Endo Pharmaceuticals	OTH
Mepact	Mepact® is designed to treat high-grade non-metastatic osteosarcoma in children, adolescents and young adults aged between 2 and 30.	Takeda Pharmaceutical Company Limited	CT
Marqibo	Marqibo® is indicated for the treatment of adult patients with Philadelphia chromosome-negative (Ph-) acute lymphoblastic leukemia (ALL) in second or greater relapse or whose disease has progressed following two or more anti-leukemia therapies.	Talon Therapeutics Inc.	CT
Copaxone	Copaxone (glatiramer) is a combination of four amino acids (proteins) that affect the immune system. Copaxone is used to treat multiple sclerosis (MS) and to prevent relapse of MS.	TEVA	ND
Myocet	Myocet is a non-pegylated liposomal doxorubicin made by Enzon Pharmaceuticals for Cephalon in Europe and for Sopherion Therapeutics in the United States and Canada. Myocet is approved in Europe and Canada for treatment of metastatic breast cancer in combination with cyclophosphamide, but is not yet approved by the FDA for use in the United States.	TEVA Pharmaceutical Industries Ltd.	CT
Fungizone®	Fungizone® Antimycotic is a formulation of amphotericin B with sodium deoxycholate as an emulsifying agent to maintain the suspension. Amphotericin B prevents the growth of fungi by causing an increase in fungal plasma membrane permeability.	Thermo Fisher	ID
Cimzia	CIMZIA (certolizumab pegol) is a tumour necrosis factor blocker (TNF blocker) indicated for the treatment of adults with moderately to severely active rheumatoid arthritis (RA).	UBC	ID

2 BIOMEDICAL MARKERS AND DETECTION AIDS

Product Name	Description	Producer	Sub-sector
CELLSEARCH® Circulating Tumour Cell Kit	The CELLSEARCH® Circulating Tumour Cell Kit is intended for the enumeration of circulating tumour cells (CTC) of epithelial origin (CD45-, EpCAM+, and cytokeratins 8, 18+, and/or 19+) in whole blood. The presence of CTCs in the peripheral blood, as detected by the CELLSEARCH® CTC Test, is associated with decreased progression-free survival and decreased overall survival in patients treated for metastatic breast, colorectal, or prostate* cancer.	Janssen Diagnostics, LLC	CT
Verigene®	Nanosphere's Verigene® System enables clinicians to rapidly identify and treat the bacteria and viruses responsible for some of the most complex, costly and deadly infectious diseases.	Nanosphere, Inc.	ID
NicAlert®	NicAlert® is an immunochromatographic assay that uses monoclonal antibody-coated gold particles and a series of avidity traps that allow quantification.	Nymox Corporation	CV
MyCare™ Assays	MyCare assays are blood tests that provide oncologists with specific information about each patient's exposure to a chemotherapy drug, helping the doctor to make informed decisions on dose adjustments. The goal of each blood test is to maximise the chemotherapy's effectiveness and limit potential side effects. MyCare is built upon the Saladax technology platform and extensive patent portfolio.	Saladax Biomedical, Inc.	CT
Stratus® CS Acute Care TM D-Dimer assay	The Stratus® CS Analyzer for acute care diagnostics provides quantitative cardiac assays for fast, accurate evaluation of patients presenting with suspected myocardial ischemia. Its efficiency and ease of use make it ideal for both point-of-care testing and lab applications.	Siemens AG Healthcare	CV

3 FERROFLUIDS

Product Name	Description	Producer	Sub-sector
NanoTherm	NanoTherm™ is a ferrofluid – a liquid that reacts to the presence of a magnetic field. The liquid acquires its magnetic characteristics from the iron oxide nanoparticles it contains. Despite an average diametre of just 15 nanometres (one nanometre is one millionth of a millimetre), the nanoparticles possess strong magnetic characteristics (known in this context as superparamagnetism).	MagForce AG	CT

4 MRI CONTRAST AGENTS

Product Name	Description	Producer	Sub-sector
Feridex IV, GastromarkCombidex, (Ferumoxtran-10)	Feridex® is a sterile aqueous colloid of superparamagnetic iron oxide associated with dextran for intravenous administration as a MRI contrast medium for the detection of liver lesions that are associated with an alteration in the RES.	AMAG Pharmaceuticals, Inc.	CT
Resovist, Supravist	MRI contrast agent for suspected liver metastases	Bayer Pharma AG	CT
NanoView MRI Contrast Agent	MRI Contrast Agent	Biophan Technologies Inc.	CT
SentiMag®	The SentiMag® instrument uses the principle of magnetic susceptometry and generates an alternating magnetic field which temporarily magnetises the iron oxide particles in Sienna+®. The tiny magnetic signature generated by the Sienna+® particles is then detected by the probe. SentiMag® offers ultrasensitive detection and location of sentinel lymph nodes with unprecedented discrimination. The system is suitable for both pre- and post-incision use, and it represents an effective radioisotope-free method of node localisation enabling the latest medical practice to be offered in a greater variety of hospitals. Sienna+® is a tracer capable of an induced magnetic response and was developed for use with the SentiMag® instrument.	Endomagnetics Limited	CT
Sienna+®	Sienna+® is a dark brown aqueous suspension of organically coated, superparamagnetic iron oxide particles. It is injected subcutaneously where the natural physical action of the lymph nodes filters out the particles, enabling the sentinel nodes to be located with the SentiMag®. For optimal localisation, agents should have a particle size range between 20 and 100 nm in diameter.	Endomagnetics Ltd	CT
Endorem, Lumirem, Sinerem	A black to reddish-brown aqueous colloid of superparamagnetic iron oxide associated with dextran for intravenous administration as a MRI contrast medium for the detection of liver lesions that are associated with an alteration in the RES.	Guerbet S.A.	CT

Product Name	Description	Producer	Sub-sector
FeraSpin	FeraSpin XL is a nanoparticulate superparamagnetic iron oxide contrast agent specifically formulated for pre-clinical magnetic resonance imaging (MRI).	Miltenyi Biotec GmbH	CT
Clariscan	An iron-based contrast agent with large molecular size, which prevents diffusion into body tissues and will be developed for MR imaging of the liver (taken up by macrophages), tumour microvasculature and microvessel permeability. The blood half live of the particles with 11-20 nm diametre is 3-4 hours.	Takeda Pharmaceutical Company Ltd	CT

5 SURFACE DISINFECTANTS

Product Name	Description	Producer	Sub-sector
EnviroTru	Disinfecting Agent	EnviroSystems Inc.	ID
Nanosept®	Disinfecting Agent	Nanobakt kft	ID
SumerSil®	Disinfecting Agent	Nano Union	ID

6 PROTEOMIC APPLICATIONS

Product Name	Description	Producer	Sub-sector
µParaflo®	Microarray services using a novel µParaflo® technology, a list of aptamer sequences, and sequence design software. The aptamer microarrays are applied for protein bindings, drug candidate screening, and biosensor engineering.	LC Sciences (Houston, TX, USA)	OTH
SOMAscan™ Assay	The latest version of the SOMAscan assay measures 1129 protein analytes in only 150 µl of several different biological matrices. The assay offers exceptional dynamic range, quantifying proteins that span over 8 logs in abundance (from femtomolar to micromolar), with low limits of detection (38 fMol media LOD) and excellent reproducibility (5.1% median %CV).	SomaLogic Inc.	OTH

7 SYNTHETIC BONE & TOOTH MATERIAL

Product Name	Description	Producer	Sub-sector
Filtek Supreme	Dental Filling Material	3M Espe	OTH
Perossal	Synthetic Bone Graft	AAP Implantate	OTH

Product Name	Description	Producer	Sub-sector
Bi-Ostetic, Cem-Ostetic	Synthetic Bone Graft	Berkeley Advanced Biomaterials, Inc.	OTH
NanoTite	Dental Implant	Biomet Inc.	OTH
Ceram X duo	Dental Filling Material	Dentspley	OTH
EquivaBone	Synthetic Bone Graft	ETEX Corporation	OTH
Mondial	Dental Restoration	Heraeus Kulzer GmbH	OTH
Ostim	Synthetic Bone Graft	Heraeus Kulzer GmbH	OTH
OsSatura TCP ® Synthetic Bone Void Filler	Synthetic Bone Graft	Isotis Orthobiologicals	OTH
Tetric EvoCeram	Dental Repair	Ivoclar Vivadent	OTH
NanOss	Synthetic Bone Graft	Pioneer Surgical Technology	OTH
CPC	Synthetic Bone Graft	Shanghai Rebone Biomaterials Co., Ltd	OTH
Vitoss	Synthetic Bone Graft	Stryker Corp. (former Orthovita)	OTH
Premise	Dental Repair	Sybron Dental Specialties	OTH

8 TRANSFECTION REAGENTS

Product Name	Description	Producer	Sub-sector
SuperFect	SuperFect Transfection Reagent is based on activated dendrimer technology developed for DNA transfection into a broad range of cell lines.	Qiagen N.V.	OTH

9 NANO-POROUS MEMBRANES

Product Name	Description	Producer	Sub-sector
Fresenius Polysulfone® Helixone®	Helixone® is the advanced high-flux polysulfone membrane of the FX-class of dialysers. Helixone® has been designed specifically to meet the present day demands of high-flux dialysis and convective therapies such as Haemodiafiltration (HDF). The Helixone® membrane is manufactured using a new process involving Nano Controlled Spinning (NCS) technology. By means of this technology it is possible to create the inner membrane layer with a defined pore structure and pore distribution profile according to the	Fresenius SE & Co. KGaA	OTH

Product Name	Description	Producer	Sub-sector
	desired application.		
Polyflux®	The Polyflux 210H dialyser offers effective removal of a wide range of middle molecules while protecting from unwanted loss of albumin. This is due to the high selectivity of its unique Polyamix™ membrane, made from a polymer blend of polyarylethersulfone, polyvinylpyrrolidone, and polyamide. The asymmetric 3-layer surface structure provides diffusive properties and sieving properties for both high-flux dialysis and convective HDF and HF treatments.	Gambro Hospal GmbH	OTH

10 ANTIMICROBIAL APPLICATIONS

Product Name	Description	Producer	Sub-sector
ON-Q SilverSoaker	ON-Q SilverSoaker Antimicrobial Catheters are impregnated with silver on both the inner and outer surfaces of the catheter. In in-vitro tests, the silver ions effectively killed organisms associated with nosocomial infections.	B. Braun Melsungen AG	ID
Nano silver iodide	Chempilots contract manufactures nano silver iodide (nAgI) that is colloidally-stabilised by PVP. The product is a powder and can be supplied with a range of silver contents (0.1-4.0 w% Ag, median particle diametre 25 nm) and PVP molecular weight.	Chempilots	ID
Acticoat	Acticoat with the nanocrystals SILCRYST™ is an antimicrobial dressing that destroys micro-organisms very rapidly and is effective against a broad spectrum of pathogens for 3 days.	Smith & Nephew plc	ID
Acticoat 7	Acticoat 7 with nanocrystals SILCRYST T™ is an antimicrobial dressing that destroys micro-organisms very rapidly and maintains its effectiveness up to 7 days.	Smith & Nephew plc	ID
Acticoat Absorbent	Acticoat Absorbent with the nanocrystals SILCRYST™ combines the antimicrobial properties of Acticoat with the advantages of a highly absorbing alginate. The dressing provides a moist environment for wound healing, is highly absorbent and releases an antimicrobial force towards the wound bed.	Smith & Nephew plc	ID

11 DRUG PRODUCTION AND MIXING SYSTEMS

Product Name	Description	Producer	Sub-sector
Microfluidizer®	High-shear fluid processors	Microfluidics Corp	OTH
Nanopure® technology	Water purification technology	Pharmasol GmbH	OTH

12 OTHER

Product Name	Description	Producer	Sub-sector
AVflo™ Vascular Access Graft	CE certified polyurethane vascular access graft, provides a high-end solution to hemodialysis patients, improving patient care and reducing hospitalisation time. The AVflo™ is the first vascular access graft to exploit the unique properties of electrospun nanofabric.	Nicast Ltd.	OTH
Betalutin	Betalutin™, is a radionuclide conjugated to a tumour seeking carrier/antibody, which can be used for irradiation of malignant metastasized tumours with minimal damage to nearby healthy normal tissue. This technology aims to prolong and improve the quality of life of people who suffer from hematologic cancer, in particular, non-Hodgkin Lymphoma (NHL).	Nordic Nanovector	CT
NanoXray	NanoXray nanoparticles were designed to increase the dose and efficacy of radiotherapy inside the tumour without causing additional damage to surrounding healthy tissues	Nanobiotix	CT
TiMESH®	The TiMESH® mesh implant is used in hernia surgery for all kinds of hernias and surgical techniques including IPOM.	PFM Medical AG	OTH

This report offers a snapshot of the environment for nanotechnology in the context of health. It gives an overview of policies and programmes for nanotechnology and health in the EU (and wider), publications, patenting, research & innovation, industry, products and markets, and the wider environment. The report is part of a series of eight NanoData Landscape Compilation studies covering the application of nanotechnology in the fields of construction, energy, environment, health, ICT, manufacturing, photonics and transport.

Studies and reports