



**Fraunhofer** Institute  
Systems and  
Innovation Research

Dr. Bärbel Hüsing  
Dr. Sibylle Gaisser

# **Nanobiotechnology in the medical sector - Drivers for development and possible impacts**

**Report for WP3: Potential socio-economic impacts  
of medicinal nanobiotechnology applications**

January 2006, revised March 29, 2006



## **Authors of the report, their contribution and affiliation**

### **WP3 coordination, Chapters 1 and 3**

Dr. Bärbel Hüsing

Fraunhofer Institute for Systems and Innovation Research

Department Emerging Technologies

Breslauer Str. 48

76139 Karlsruhe

Germany

E-Mail: [baerbel.huesing@isi.fraunhofer.de](mailto:baerbel.huesing@isi.fraunhofer.de)

Phone: +49-721-6809-210

### **Chapter 2: Impacts of nanotechnology on health care costs**

Dr. Sibylle Gaisser

Fraunhofer Institute for Systems and Innovation Research

Department Emerging Technologies

Breslauer Str. 48

76139 Karlsruhe

Germany

E-Mail: [sibylle.gaisser@isi.fraunhofer.de](mailto:sibylle.gaisser@isi.fraunhofer.de)

Phone: +49-721-6809-205

### **Project assistance, secretary**

Silke Just

Fraunhofer Institute for Systems and Innovation Research, Department Emerging Technologies, Karlsruhe, Germany



## List of contents

<b>1</b>	<b>Objective</b> .....	<b>1</b>
<b>2</b>	<b>Impact of nanobiotechnology applications on health care costs</b> .....	<b>3</b>
2.1	Introduction .....	3
2.2	Methodology .....	4
2.3	Future trends in the health system .....	6
2.4	Relevance of nanotechnology in the health care system .....	20
2.5	Effects of nanotechnological products.....	21
2.6	Case study 1: Liposomal amphotericin B (AmBisome®).....	24
2.7	Case study 2: Pegylated liposomal doxorubicin hydrochloride .....	26
2.8	Conclusions .....	28
2.9	References.....	31
<b>3</b>	<b>Social and ethical issues in nanobiotechnology in the medical sector</b> .....	<b>35</b>
3.1	Introduction .....	35
3.2	Human health impacts .....	37
3.3	Environmental impacts.....	43
3.4	Health and environmental risks associated with nanoparticles.....	46
3.5	Equal access and just allocation of resources .....	49
3.6	Privacy .....	54
3.7	Regulation, control, liability .....	59
3.8	Governance .....	62
3.9	Enhancement.....	64

3.10	Blurring the borderline between humans and technical artefacts .....	67
3.11	Military uses .....	70
3.12	Public perception of and attitudes towards nanotechnology and nanobiotechnology in the medical sector .....	71
3.13	Conclusions.....	93
3.14	References.....	96
<b>4</b>	<b>Annex.....</b>	<b>107</b>
4.1	Email survey, conducted for chapter 2 .....	107
4.2	Health economics experts contacted in the frame of the email survey in chapter 2 .....	108
4.3	Experts interviewed for chapter 3.....	110

## List of tables

Table 2.1:	Search terms for health economic publications.....	4
Table 2.2:	Old age dependency ratio in EU member states, 1995-2050.....	10
Table 2.3:	Expected days of inpatient care for disease groups in Germany 2020.....	14
Table 2.4:	Average days spent in hospital by diagnosis in 1999.....	16
Table 2.5:	Expected costs for different disease groups in Germany in 2020 .....	18
Table 2.6:	Aspects of process and product innovation.....	20
Table 2.7:	Technological fields with nanotechnology relevance in the field of health care .....	21
Table 3.1:	Possible positive and negative environmental impacts deduced from basic characteristics of nanotechnologies .....	44
Table 3.2:	Overview of published studies on media coverage of nanotechnology .....	72
Table 3.3:	Overview of surveys of the general public's knowledge of and attitudes to nanotechnology .....	76
Table 3.4:	Selected focus groups on nanotechnology.....	82
Table 3.5:	Citizens' juries on nanotechnology .....	84
Table 3.6:	Concerns related to nanotechnology, as identified in workshops with 177 US citizens.....	86
Table 3.7:	Recommendations made by the UK citizens' jury on nanotechnology in autumn 2005 .....	88

**List of figures**

Figure 2.1:	Population in Germany in thousands 2002, 2020 and 2050 .....	8
Figure 2.2:	Population growth rates .....	8
Figure 2.3:	Life expectancy at birth .....	9
Figure 2.4:	MDC-based group costs differentiated by cost origin, based on German hospital cost data in 2002 .....	19

# 1 Objective

In the last decade, nanotechnologies applications in the medical sector ("nanomedicine") have seen both a surge in research activity as well as the start of commercialisation efforts around the world. Nanomedicine comprises seven application fields: drug delivery, drugs and therapies, in vivo imaging, in vitro diagnostics, implant materials, active implants, and cosmetics.

Against this background the European Commission published a proposal for a European strategy<sup>1</sup> and an Action Plan<sup>2</sup>, aiming at a co-ordinated R&D approach to nanotechnology to be able to exploit the benefits of this new technology and its applications. The Commission highlighted the need to examine and map existing research infrastructure, to identify the most urgent needs to accelerate progress in nanotechnology, and stressed the need for a prospective view regarding emerging developments. It emphasised the necessity to assess and address the public's perception and acceptance, to identify and address safety concerns, and to monitor and share information related to scientific, technological, economic, and social development in nanotechnologies.

On request of DG Enterprise, the JRC Institute for Prospective Technological Studies commissioned the study "Nanobiotechnology in the medical sector - Drivers for development and possible impacts" with the aim to provide policy-relevant information on the applications of nanobiotechnology in the medical devices and the pharmaceutical sectors. The study comprised three work packages. It was the aim of work packages 1 and 2 to give a comprehensive picture on academic nanomedicine research and commercial activities in Europe, and to identify drivers. This analysis has been performed by Zukünftige Technologien Consulting, Düsseldorf and has been documented in a separate report (Wagner, Zweck 2005).

---

<sup>1</sup> Communication from the Commission: Towards a European Strategy for nanotechnology. COM (2004) 338 final.

<sup>2</sup> Communication from the Commission: Action Plan "Nanosciences and nanotechnologies: An action plan for Europe 2005-2009". COM (2005) 243 final.

It was the aim of work package 3 to identify and analyse the potential socio-economic impacts of medicinal nanobiotechnology applications by focussing on the following questions:

- How will nanobiotechnology impact the health care costs (chapter 2)?
- Which social and ethical issues are to be considered with regard to novel applications of nanobiotechnology in the medical sector (chapter 3), taking into account
  - What are the environmental and health risks of medicinal nanobiotechnology applications, considering the whole life cycle of products?
  - What is the attitude of the public and of main non-governmental organisations (NGOs) towards medicinal nanobiotechnology?

The results of work package 3 of the project "Nanobiotechnology in the medical sector – Drivers for development and possible impacts" are presented in this report.

## **2 Impact of nanobiotechnology applications on health care costs**

### **2.1 Introduction**

Nanobiotechnological developments promise several applications that will improve health care. Among them are drug delivery systems that allow the site-directed application of a pharmaceutical, novel drugs to cure cancer, cardiovascular diseases and neurodegenerative diseases. Microarrays will allow more precise and earlier diagnosis which will help to initiate treatment before a disease becomes clinically apparent and thus alter curative medicine into preventive medicine. Finally it is expected that nanotechnological implants will have improved durability and better tissue compatibility.

However, are all these developments affordable for the health system in general? How will nanobiotechnological products impact health care costs and can nanobiotechnology compete with conventional products in the medical sector?

Still, impact on health spending and cost effectiveness of nanotechnological products is very difficult to predict. This owes to the fact that only few first generation products are on the market. Because these products are used in various areas of indications it is impossible to conduct an overall health technology assessment including cost effectiveness and cost benefit studies. Up to now, evaluations have been conducted on a case by case basis. Apart from the limited number of products different application schemes in different countries allow only limited transferability of study results from one country to another. Although national health technology assessment institutions try to develop a methodology that allows the translation of foreign study results into the own national context (Siebert 2005) this lack of comparability of national health care systems leads to a huge demand for national health technology assessment studies.

It is the aim of the study to gain insights into expected impacts of nanobiotechnological products on the health care costs in the most relevant disease groups and show in two case studies their present and future competitiveness by the synopsis and evaluation of cost-effectiveness and cost-benefit studies.

## 2.2 Methodology

### 2.2.1 Literature review

On the basis of WP 1 and 2 (Wagner, Zweck 2005) and of the study “Nanotechnology pro Health: Chances and Risks” (Farkas et al. 2004) carried out on behalf of the German Research Ministry (BMBF) a search term list was developed. This list was used to identify cost effectiveness, cost benefit studies and general cost analyses in the field of nanobiotechnological applications. The search terms are listed in Table 2.1 and were combined by Boolean operators to delineate the field of nanotechnology.

Table 2.1: Search terms for health economic publications

Indication	Application	Focus of study
neoplasms	biochips	cost effectiveness
infectious diseases	microarray	cost benefit
cardiovascular diseases	liposomes	cost analysis
neurodegenerative diseases	drug delivery	expenditures
muscle and skeletal diseases	implant	
	biosensor	
	endoprosthesis	

The literature search was carried out in the MEDLINE database<sup>3</sup>, in the Scopus database<sup>4</sup>, in the Cochrane Library<sup>5</sup>, the NHS Centre for Reviews and Dissemination Database (NHS CRD)<sup>6</sup>, and the database of the German Agency for HTA<sup>7</sup>. It was complemented by manual literature search and internet searches. The MEDLINE database is the most extensive database on medical research literature and covers all fields of medicine, including nanotechnology as well as health economy. The Scopus database is a product of Elsevier covering over 14,000 peer reviewed titles in the field of natural science, medicine, economy and social science. The Cochrane Library is a database that specialises in structured reviews (meta-analyses) of medical therapies and as a sub-division includes health technology assessments (HTAs) which normally report

3 <http://www.ncbi.nih.gov/entrez/query.fcgi>

4 <http://www.scopus.com>

5 via the German Network on Evidence-Based Medicine

6 <http://agatha.york.ac.uk/welcome.htm>

7 <http://www.dimdi.de/static/en/hta/db/index.htm>

cost-effectiveness data. The NHS CRD database lists national (UK) and international HTAs and economic evaluations.

The search strategy for the case studies included a top-down approach based on the indications as key words which represent the MeSH-Terms<sup>8</sup> in the MEDLINE and Cochrane Database combined with relevant nanobiotechnological applications and the MeSH-terms for cost and cost-effectiveness (Table 2.1). In a second approach, which was a bottom-up search nanobiotechnological products as identified by Wagner, Zweck 2005 were combined with the respective key words and MeSH-terms for cost and cost-effectiveness studies (Table 2.1). In order to make sure that no important economic analysis of nanotechnological products had been overlooked, the health economists addressed in the quality control step were also asked to provide information on relevant studies known to them.

In MEDLINE, a total of 717 articles were identified. Because this number was too high to be scanned manually, only the most recent articles, published between 2000 and 2005, were analysed (346 articles). In the Cochrane Library 167 articles had to be scanned manually. After reviewing the abstracts, 23 articles from MEDLINE, 10 from the Cochrane Library and a few from the other sources were analysed in depth. 10 articles dealt with pegylated liposomal doxorubicin, six with liposomal amphotericin B<sup>9</sup>, 10 articles dealt with other cases, especially drug delivery and microarrays. The two cases with a significant number of detailed publications (pegylated liposomal doxorubicin, liposomal amphotericin B) were chosen as case studies, the results of the remaining publications were integrated in the overall description of the indications. Articles identified in the literature search, that did not analyse cost aspects but technological options were not integrated into this study.

### **2.2.2 Expert interviews**

In order to validate the results from our literature analysis, 25 experts with a health economy background from 10 European countries were chosen to comment on the results of the literature survey. The experts were identified by internet search. Some of them were known to us from previous projects in the field of novel medical developments. Addressing the experts via email and personal communication, they were asked to comment on the results of the German analysis as presented by Farkas et al. 2004, on the results of the literature analysis and to compare the described effects with their

---

8 MeSH: Medical Sub-Heading in the structured hierarchical thesaurus.

9 The number of articles for each case study does not add up to the total number of articles identified as some duplicates were identified from the databases.

national situation and personal assessment of the European situation (for details, see annex).

Helpful comments were received from four experts from the Netherlands, Switzerland, Ireland and Italy. Seven did not feel competent to answer the questions, four were under time restrictions that hindered them to answer, 10 did not at all reply to the questionnaire. The poor response rate shows the difficulty in gathering health economic data in the very early stage of development in which nanotechnology in the medical sector is still.

### **2.2.3 Indicator-based quality control**

Because the German study only analyses possible health care impacts for the German situation, an attempt was undertaken to assess the relevance of the findings from Germany for Europe. The validity of the underlying assumptions for Europe was analysed with the help of the European Community Health Indicators (ECHI) (European Commission 2005). Under the EU Health Monitoring Programme (HMP), several ECHI projects resulted in the establishment of a set of appr. 400 indicators (status of June 2005) that will serve as a basis for the European health information and knowledge system in order to facilitate the monitoring of trends, differences and policy impact throughout the EU<sup>10</sup>.

## **2.3 Future trends in the health system**

### **2.3.1 Background information**

In historical perspective, innovations in medical technology were predominantly incremental innovations, with few major innovations (e. g. X ray, antibiotics, chemotherapy) in the 20<sup>th</sup> century, resulting in significant gains in life expectancy and quality of life. Despite intensive research, only moderate improvements in morbidity and mortality in the major diseases have been achieved in industrial countries in the last decades, due to the complexity of the underlying diseases and the fact that a large share of the population can now approach the end of their biologically determined life span. Against this background, it is understandable that present medical innovations are mostly incremental innovations which offer a measurable, albeit but only small health effect at significant costs. It is a generally valid observation that, in terms of the cost-benefit-ratio, the majority of new interventions does not perform better than the established interventions that they replace. By contrast, innovations which offer a significant medical bene-

---

<sup>10</sup> [http://europa.eu.int/comm/health/ph\\_information/dissemination/echi/echi\\_en.htm](http://europa.eu.int/comm/health/ph_information/dissemination/echi/echi_en.htm)

fit, and in addition are even cheaper than established interventions, occur only rarely today (Farkas et al. 2004, p. 159).

In most industrial countries, rising health expenditures are a major problem of the health system. The most prominent explanations for this fact are the demographic changes and the high costs of innovations.

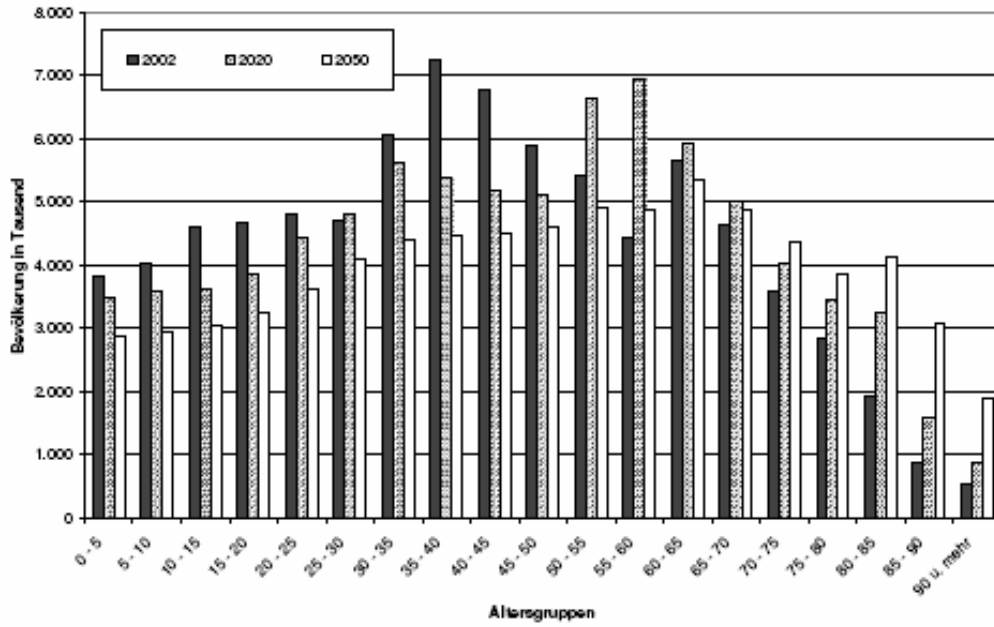
### **2.3.2 Population development and health care expenditure**

The aim of this chapter 2 is to assess the possible impacts of nanomedicine on health care expenditure. Because nanomedicines are in an early stage of development and will become available in the clinic on a broader scale not before several decades time, their impact on *future* health care expenditure and coverage has to be assessed. However, future health care expenditure depends on a number of influencing factors, among them the absolute number of persons in a given population, their age distribution and health status, which, to some extent, can also be expected to be age-dependent.

The following analyses show that the population in Europe will be ageing significantly in the coming years: Projections for Germany show an increase in both the absolute number of old and very old people, and also in their share of the total population in the future. The number of people in the group of 80 years and older is expected to double between 2002 and 2050 (Figure 2.1). The ageing of society can not only be observed in Germany but in most industrialised countries, as shown in an analysis of the OECD (OECD 2002). The main reasons for the ageing of society are the decline in fertility and population growth rates (Figure 2.2) and the increases in life expectancy at birth (Figure 2.3).

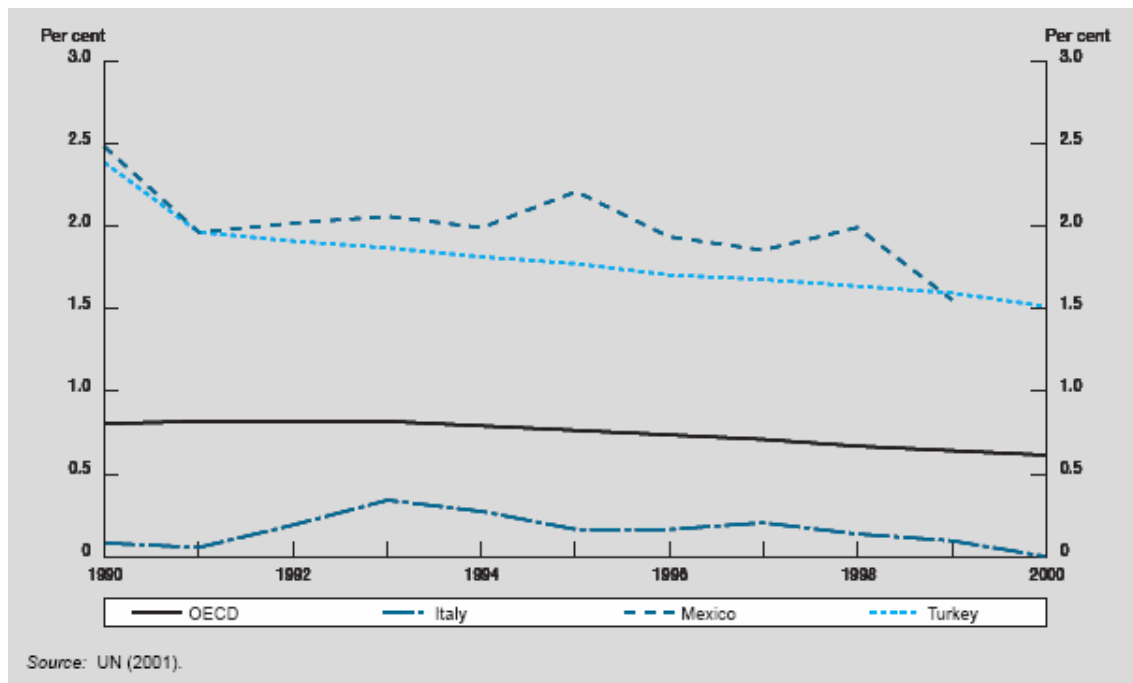
This changing age structure of the society challenges the sustainability of social security systems, such as the health care system or pension systems, because most of these systems are based on a pay-as-you-go financing mode. Because of this mode, population ageing unbalances the relation between health care expenditures and health care contributions, because fewer people of working age will have to support those in retirement. This is reflected by the indicator of old-age dependency.

Figure 2.1: Population in Germany in thousands 2002, 2020 and 2050



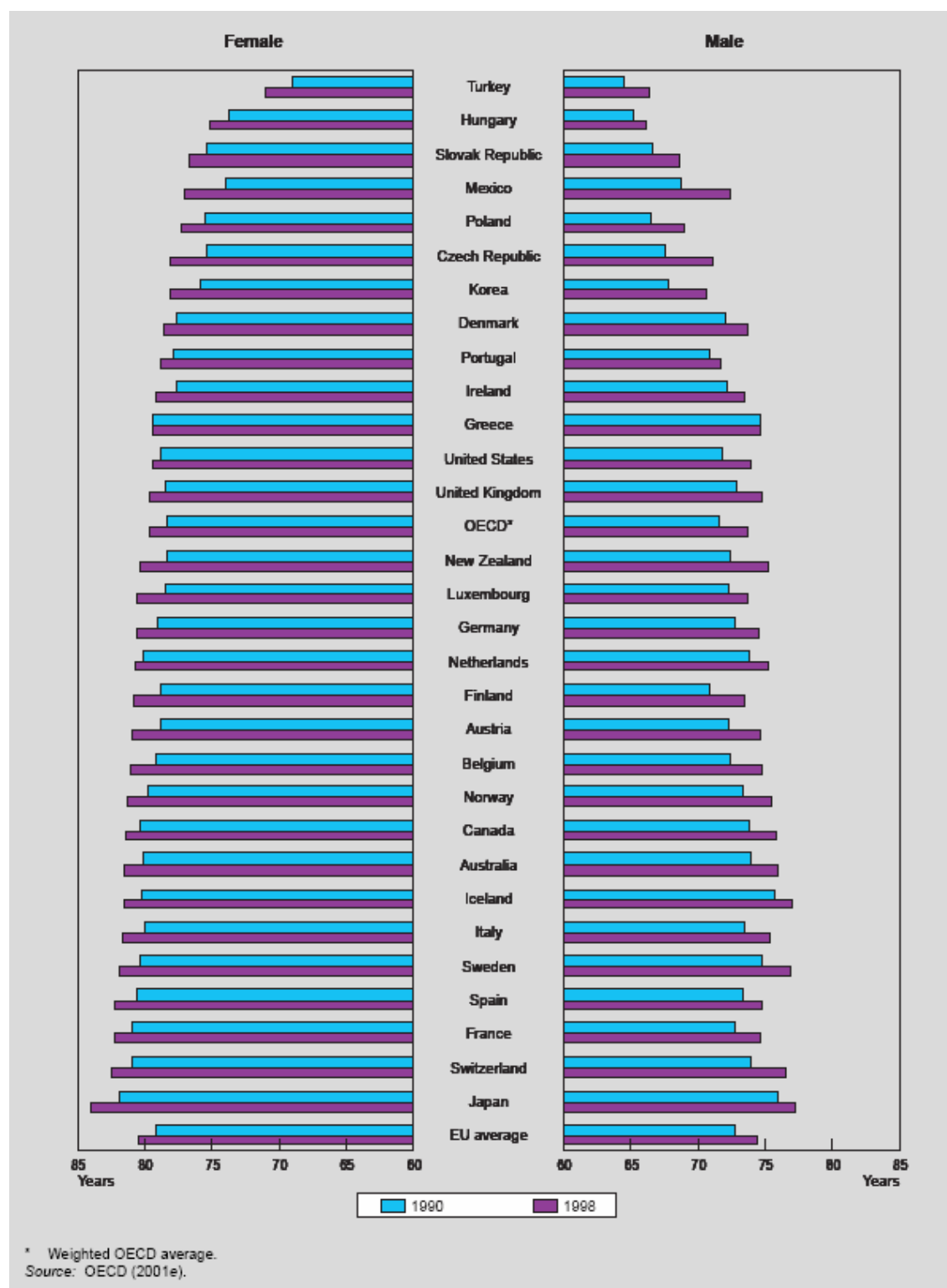
Source: German Statistical Office, Calculations by AGIT 2004

Figure 2.2: Population growth rates



Source: OECD 2002

Figure 2.3: Life expectancy at birth



Source: OECD 2002

The old age dependency ratio is the ratio between the total number of elderly persons of an age when they are generally economically inactive (aged 65 and over or aged 60 and over, depending on the context) and the number of persons of working age (from 15 to 64 or from 20 to 59, depending on the context). As shown in Table 2.2, the old age dependency ratio is expected to rise in the old EU member states (EU 15) from 23 in 1995 to 47.2 in 2050. There are some differences between countries: Some states such as Spain and Italy have an age dependency ratio above 50, others at the opposite end of the spectrum such as Denmark, Luxemburg and Sweden are below 40 (Table 2.2).

Table 2.2: Old age dependency ratio in EU member states, 1995-2050

	1995	2000	2010	2020	2050
EU (15 countries)	23.0	24.1	27.0	31.7	47.2
Austria	22.4	22.6	25.6	28.5	44.3
Belgium	23.8	25.4	26.9	32.6	43.5
Denmark	22.7	22.1	24.3	30.1	37.7
Finland	21.1	21.9	24.7	35.0	42.1
France	22.9	24.3	25.5	32.6	46.4
Germany	22.5	23.3	29.2	31.9	46.8
Greece	22.8	25.5	29.3	32.3	48.0
Ireland	18.0	17.4	18.5	24.5	43.6
Italy	24.0	26.5	31.0	35.5	55.7
Luxembourg	20.6	21.5	23.5	27.9	37.8
Netherlands	19.3	20.1	22.5	29.8	40.7
Portugal	21.4	22.5	24.3	27.3	44.0
Spain	22.2	24.4	26.5	29.8	56.5
Sweden	27.4	26.8	27.9	33.4	37.9
United Kingdom	24.3	24.0	24.7	29.8	42.8

Source: European Commission, DG Health and Consumer Protection (2005);

[http://epp.eurostat.ec.eu.int/portal/page?\\_pageid=1996,39140985&\\_dad=portal&\\_schema=PORTAL&screen=detailref&language=en&product=sdi\\_as&root=sdi\\_as/sdi\\_as/sdi\\_as1000](http://epp.eurostat.ec.eu.int/portal/page?_pageid=1996,39140985&_dad=portal&_schema=PORTAL&screen=detailref&language=en&product=sdi_as&root=sdi_as/sdi_as/sdi_as1000)

But what will be the impacts of an ageing population on health care expenditure? The view that health care expenditure is simply a function of age alone (in the sense of

"health care expenditure increases with age") is heavily debated nowadays. Additional factors have to be taken into account, among them

- substantially higher health care expenditures in the last year of life, than for "survivors" of the same age. There is evidence that the absolute health care expenditure is determined by both proximity to death and age, and not age alone. According to this "hypothesis of compression", people produce the highest costs in the year of their death.
- future gains in life expectancy. There is uncertainty whether gains in life expectancy will decrease because the approach biological limits, or whether they continue to be realised,
- health status of the population. There is uncertainty whether the future health status will remain at a constant level per age group (thus leading to a decline in the health status of the total population as the population ages), will decrease with age (e. g. due to worsening health because of overweight and unhealthy life styles), or whether elderly will show an improved health status ("healthy ageing").

Model projections for the future development of health care expenditure were calculated by the Netherlands Bureau for Economic Policy Analysis (CPB) within the AGIR project 2002<sup>11</sup>. These projections were based on demographic data taken from the Eurostat 2000 population projections, and assumed that healthcare expenditures would rise in line with GDP. In different scenarios, the researchers considered not only variations on health expenditure by age, but also lower healthcare costs for survivors than for decedents in the same age group, and different health states of the population.

In 2002, the average total public expenditure on healthcare (including both curative activities and long-term care) amounted to 6.2 % in the EU-15 countries. The model projections performed by the Netherlands Bureau for Economic Policy Analysis (CPB) indicate that this figure can be expected to increase to 7.2 % in 2020 and to 8.9 % in 2050. Because of national specificities in demographic development and health care systems, the increase in health expenditure is expected to be particularly dramatic in certain countries, and to reach the 10 % level of GDP in countries such as Sweden, Finland and the Netherlands by 2050, under the current institutional framework and expenditure patterns (Surcke et al. 2005).

---

<sup>11</sup> AGIR (acronym for 'Ageing, health and retirement in Europe') is the name of a three-year European research project on the economic consequences of ageing. It was financed by the European Commission under the fifth research framework programme. Researchers from nine European economic policy research institutes have participated in this project. The AGIR project has explored all available information on the health developments in the EU-15 countries during the last 50 years, and analysed how different future demographic and health scenarios could affect pension and healthcare expenditure in several EU countries. Further information on this project can be found at: <http://www.enepri.org/Agir.htm>

The possible impact of the "compression of morbidity hypothesis" on expenditure was also projected in an optimistic 'living in better health scenario', which assumes that in the next 50 years the number of years lived in bad health will be kept at the current level (and that therefore all improvements in life expectancy would lead to years lived in good health). In this scenario, the level of health care expenditure would rise to 8 % of GDP in EU-15 by 2050. This increase is, however, 0.9 % of GDP lower than in the baseline scenario (8.9 % in 2050). This further highlights the importance of investing in population health as a means of mitigating future economic impacts of ageing populations (Surcke et al. 2005).

All in all, these above cited model projections show that it will become difficult in the future to finance health innovations which will result in an increase of health care expenditure. On the other hand, health innovations will be most welcome which bear the potential to reduce health care expenditure, either by cost savings in interventions, or by keeping people healthy longer. In the following subchapters, it will be analysed whether and to which extent nanomedicine bears the potential to contribute to a reduction of health care expenditure.

### 2.3.3 Cost development and cost drivers

In order to analyse the possible future impacts of nanomedicine on future health care expenditure, the main cost drivers in health care expenditure must be identified. Then it can be analysed to which extent nanomedicine is likely to influence these cost drivers. because the cost impact of nanomedicine can be assumed to be large if it influences the main cost drivers.

#### Model calculation 1

One approach, taken by Farkas et al. 2004 for Germany, is to estimate the future treatment costs by multiplying present treatment costs with demographic factors for each age group. Because no direct data for present treatment costs were available, Farkas et al. 2004 used days of inpatient care as a surrogate. Days of inpatient care are seen as an acceptable measure for the required intensity of care and the resulting treatment costs. In 1999, a total of 170 mio. days in hospital were spent in Germany. 102 mio. of them were required for the group of old and very old people (55 years and older), so that approximately 60 % of the days in hospital are required for 30 % of the population. It is obvious that intensity of care and treatment costs differ from disease to disease. Therefore, a differentiation according to disease groups (using the ICD classification<sup>12</sup>) was carried out. The results of this analysis are shown in Table 2.3: Compared to 1999, the days in hospital are expected to increase from 170,000 to 195,000 and thus by 14.5 % until 2020. Neoplasms (II), psychiatric diseases (V), and cardiovascular diseases (VII) are expected to become the three diagnose categories with the highest number of days in hospital in Germany in 2020. The largest relative increase in days of inpatient care is expected for cardiovascular diseases (VII), diseases of the haematopoietic system (IV), Endocrine, nutritional and metabolic diseases (III) and neoplasms (II) (Querverweis). So, cardiovascular diseases and neoplasms are of major importance in this respect, because they are not only expected to cause the largest number of days in hospital, but also to show the largest relative change between 1999 and 2020.

---

<sup>12</sup> ICD = International Classification of Diseases. Elaborated by the World Health Organisation (WHO), the ICD has become the international standard diagnostic classification for all general epidemiological and many health management purposes. It is used to classify diseases and other health problems recorded on many types of health and vital records including death certificates and hospital records. In addition to enabling the storage and retrieval of diagnostic information for clinical and epidemiological purposes, these records also provide the basis for the compilation of national mortality and morbidity statistics by WHO Member States.

Table 2.3: Expected days of inpatient care for disease groups in Germany 2020<sup>13</sup>

Disease group (according to the ICD)	Days of inpatient care in Germany			
	1999	Projection 2020	Change 1999 to 2020	Change in %
I. Infections	2,792,980	3,073,193	280,213	10.0
II. Neoplasms	19,810,576	23,468,035	3,657,459	18.5
III. Endocrine, nutritional and metabolic diseases	5,037,109	5,966,726	929,617	18.5
IV. Diseases of the haematopoietic system	991,339	1,216,591	225,252	22.7
V. Psychiatric disease	22,912,233	23,215,944	303,711	1.3
VI. Diseases of the nervous system	7,897,594	8,912,088	1,014,494	12.9
VII. Cardiovascular diseases	31,153,603	39,435,693	8,282,090	26.6
VIII. Diseases of the respiratory system	9,364,241	10,811,494	1,447,253	15.5
IX. Diseases of the digestive sys- tem	14,280,659	16,367,966	2,087,307	14.6
X. Diseases of the genitourinary system	7,513,199	8,469,510	956,311	12.7
XI. Complications of pregnancy, delivery, puerperium	6,132,848	5,612,765	-520,083	-8.5
XII. Diseases of the skin, subcuta- neous tissue	2,929,547	3,282,216	352,669	12.0
XIII. Diseases of the skeleton, muscles, connective tissue	14,392,246	16,530,092	2,137,846	14.9
XIV. Congenital diseases	967,059	904,590	-62,469	-6.5
XV. Certain affections originating in the perinatal period	1,592,247	1,465,346	-126,901	-8.0
XVI. Symptoms, poorly denomi- nated affections	4,387,757	5,214,056	826,299	18.8
XVII. Injuries, intoxications	16,539,846	19,229,646	2,689,800	16.3
Without diagnosis	228,092	253,583	25,491	11.2
Other factors that influence the health status	864,791	936,518	71,727	8.3
Total	169,787,966	194,366,053	24,578,087	14.5

Source: Farkas et al. 2004 (calculations on basis of the German statistical office)

<sup>13</sup> The days of inpatient care were calculated on basis of the numbers given in the official hospital statistics of the year 1999 multiplied with the demographic factor taken from coordinated population prognosis. This model allowed the estimation of inpatient care in the year 2020 for specific diagnose groups (Farkas et al. 2004).

In order to check whether these projections for Germany can, at least in tendency, be extrapolated to Europe, European data on the average lengths of stay in hospital were analysed<sup>14</sup> (Table 2.4). They show that neoplasms, cardiovascular diseases, musculoskeletal diseases and in some countries respiratory diseases are an important factor in health expenditures according to average length of stay in hospital: On average, patients with malignant neoplasms are discharged from hospital after 10.2 days, patients with cardiovascular disease after 9.6 days, patients with musculoskeletal diseases after 9.1 days and patients with respiratory disease after 7.7 days. The numbers for Germany are slightly above the average. From this it can be concluded that the results about health economic impact of nanobiotechnology which were gained from underlying assumptions drawn from the German health economic analysis by Farkas et al (2004) will in principle apply also for most European countries.

In countries with very short stay in hospital such as the United Kingdom, Denmark, Luxembourg, Norway, Sweden and Turkey, the health economic impact of nanobiotechnology will most likely be smaller than in countries with more days of in-patient care such as Belgium, the Netherlands, Ireland, and Germany. This is due to the fact that in the former countries, nanotechnologies-enabled innovations that help to reduce the number of days in hospital can contribute only to a smaller reduction of the average time in hospital. Further details are described below.

---

<sup>14</sup> The year 1999 was chosen from the set of data because it contained data for most countries. For some countries information was only available for other years than 1999. In these cases the reference year is indicated in brackets after the country name.

Table 2.4: Average days spent in hospital by diagnosis in 1999

Diagnose group	Malignant Neoplasms	Cardio-vascular Diseases	Respiratory Diseases	Musculo-skeletal Diseases	Pregnancy, Childbirth and Puerperium
Country					
Austria	7,1	14,1	8,9	11,2	5,6
Belgium (1998)	12,5	9,9	9,2	12,0	5,6
Bulgaria (2000)	13,4	12,6	11,5	14,6	5,3
Cyprus	9,7	7,4	5,5	9,6	6,2
Czech Republic	10,4	10,0	7,1	9,6	5,9
Denmark	7,4	7,5	5,5	7,5	3,4
Estonia	10,2	11,0	7,8	10,5	4,3
Finland	7,7	15,6	11,3	6,0	3,6
France (1997)	10,2	7,7	6,8	7,2	5,5
Germany	11,0	11,3	7,8	10,5	5,8
Greece	12,5	7,3	5,3	8,0	4,4
Hungary	9,4	10,2	7,7	11,7	5,2
Ireland	13,4	10,8	7,1	9,0	3,9
Italy	11,7	8,3	7,5	7,0	4,4
Latvia	11,9	10,4	9,5	12,4	5,8
Lithuania	12,9	13,0	9,4	12,1	5,4
Luxembourg	9,0	8,7	5,6	5,8	4,3
Malta (2000)	6,9	7,0	5,1	6,9	3,3
Netherlands	11,2	10,5	9,1	9,2	4,5
Norway	8,8	6,6	6,2	7,2	4,4
Poland	11,7	11,4	11,2	16,1	6,3
Portugal	13,3	8,5	8,4	8,8	3,6
Romania	10,5	10,5	8,9	11,8	4,7
Slovakia	10,3	10,5	8,0	10,4	6,9
Slovenia	11,4	10,5	8,8	10,1	4,9
Spain	12,5	9,8	8,2	7,4	3,8
Sweden	7,9	6,7	5,4	6,8	3,2
Turkey	9,9	6,4	6,1	3,3	10,2
United Kingdom	4,2	8,7	6,4	7,2	1,9
United States	7,0	4,9	5,4	4,3	2,6
<b>Average</b>	<b>10,2</b>	<b>9,6</b>	<b>7,7</b>	<b>9,1</b>	<b>4,8</b>

Source: European Commission 2005;

[http://europa.eu.int/comm/health/ph\\_information/dissemination/echi/echi\\_22\\_en.pdf](http://europa.eu.int/comm/health/ph_information/dissemination/echi/echi_22_en.pdf)

## Model calculation 2

Model calculation 1 has the disadvantage that future health care expenditure is assessed on the basis of days of inpatient care, but not on cost information. To overcome this limitation, Farkas et al. 2004 performed a second model calculation in which – preliminary – cost information was used. The approach was similar to model calculation 1: Cost information was multiplied with demographic factors for each age group in order to calculate future health care costs per disease group in 2020. The cost information used were actual cost data from a sample of German hospitals which were used to calculate flat rates for the respective diagnosis-related groups<sup>1516</sup>. On this basis, Farkas et al. (2004) modelled a prognosis for future health care costs in 2020. According to this calculation, the highest costs are expected for diseases of the nervous system (MDC1 (major diagnosis category 1)), cardiovascular diseases (MDC 5), diseases of the digestive system (MDC 6), and diseases of the musculoskeletal system and connective tissue (MDC8) (Table 2.5). For each of these disease groups, health care expenditures are expected to increase between 20-30 % in the coming 20 years. Neoplasms, identified in model calculation 1 as a major cost driver, do not form a separate DRG and therefore their expected cost change over time cannot be estimated with model calculation 2.

---

<sup>15</sup> Cost information was derived from the first calculation of average costs per case for so-called diagnosis-related groups, published in September 2002. The sample on which the cost calculations were based corresponded to 3 % of all cases treated in hospitals, and to 5 % of all hospitals in Germany.

<sup>16</sup> Diagnosis-related groups is a classification scheme with which to categorize patients according to diagnoses, similar clinical conditions and expected treatment costs. This classification scheme is used to pay a hospital for their services. In Germany, hospitals are paid a fixed flat rate per case in a given diagnosis-related group, irrespective of the actual treatment costs for the individual case.

Table 2.5: Expected costs for different disease groups in Germany in 2020<sup>17</sup>

DRG-group	Number of days of inpatient care (2001)	Total costs (2001) <sup>12</sup>	Expected costs (2020) <sup>12</sup>	Change 2001/2020
MDC <sup>18</sup> 8: Diseases of the musculoskeletal system and connective tissue	747.894	92.478,97	110.429,32	19,41 %
MDC 5: Cardiovascular diseases	548.663	74.077,20	97.630,27	31,80 %
MDC 6: Diseases of the digestive system	407.504	50.100,16	60.264,49	20,29 %
MDC 1: Diseases of the nervous system	387.917	42.355,48	52.541,45	24,05 %
MDC 4: Diseases of the respiratory system	358.855	34.925,66	43.487,34	24,51 %
MDC 9: Diseases of skin, subcutaneous tissue and breast	154.834	17.141,02	20.052,97	16,99 %
MDC 7: Diseases of hepatobiliary systems and pancreas	148.379	16.803,82	20.000,73	19,02 %
MDC 3: Diseases of ear and mastoid process	140.211	16.424,90	16.796,18	2,26 %
MDC 2: Diseases of the eyes	58.872	8.268,05	11.069,37	33,88 %

Source: Farkas et al. 2004 (calculation on basis of DRG first calculations (www.g-drg.de), statistical office of Germany)

### Model calculation 3

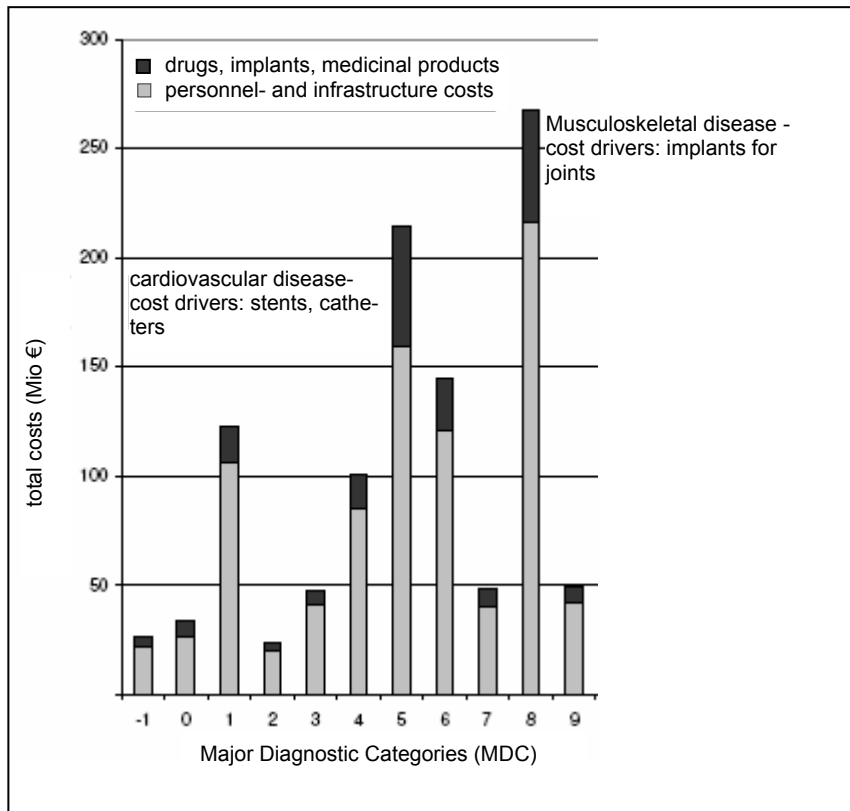
A third analysis, performed by Farkas et al. 2004, aimed at identifying the major costs for a given disease group according to their origin. They used the DRG-case-cost calculation data which had also been used in model calculation 2. All costs that are primar-

<sup>17</sup> The costs are given in dimensionless figures. The value 1 equals an average hospital case which is rated with € 2.900 per case.

<sup>18</sup> MDC: Major diagnosis category. The German DRG catalogue is divided into chapters, the major diagnosis groups, which structure the DRGs with respect to the organ system or the cause of the disease.

ily determined by technology, i. e. drugs, implants, medicinal products were summarised in one category which was compared to costs for personnel and infrastructure (Figure 2.4). It turned out that the technology-dependent costs were a maximum of 20 % of the total costs (Farkas et al. 2004).

Figure 2.4: MDC-based group costs differentiated by cost origin, based on German hospital cost data in 2002



Source: Farkas et al. 2004

From these results, Farkas et al. concluded the following: As technology dependent costs such as drugs, implants and medicinal products contribute only to a small proportion to the total costs in the health care system, nanotechnological innovations will impact health care costs only significantly if they act indirectly on personnel and infrastructure costs. Those innovations that will allow a reduction of the time spent in hospital will have the potential to reduce the personnel costs and thus reduce the total health care costs. By contrast, those nanotechnological innovations that act only on the technological level are likely to have little effect on health expenditures because technology dependent costs are apprx. only 20 % of total costs. Provided, that observation in the past from medical innovations can be transferred to nanomedical innovations as well, it

can be expected that most innovations come as add-on technologies which in most cases act as a cost driver for the health system or are at best cost neutral (see also chapter 2.3.1) (Farkas et al. 2004).

Two types of innovations can be identified: process innovations and product innovations. As described by Zweifel (2003) the willingness and openness of consumers and physicians/hospitals to adopt an innovation differ between the two types of innovations. As long as patients are fully insured and gain no profit out of cheaper or more efficient therapy by a process innovation but hope to get a better treatment by a product innovation they will prefer product innovations. Similarly, hospitals cannot attract patients by cheaper or more cost-efficient therapies but by the offer to use novel product innovations. Of course this changes if insurers had the right to engage in selective contracting or if a hospital is under financial pressure due to high costs for personnel costs.

The lack of interest in process innovations finally influences the strategic positioning of medical suppliers such as pharmaceutical companies. They are hesitant to invest in new products that promise to reduce the cost of service in hospital and medical practices (Zweifel 2003). This behaviour is a significant barrier to positive cost impacts of nanotechnological products with process innovation characteristics.

Table 2.6: Aspects of process and product innovation

Aspect	Process innovation	Product innovation
Basic idea	The same process, but less costly and/or faster	New attributes, may also cost more
Consumer's willingness to pay	Unchanged	Increased and enhanced by a limited monopoly (patents)
Response within the user group	Considerable resistance	Support
Market result	The mix of the two types of innovation depends on cost-benefit considerations on the part of consumers	

Source: Zweifel 2003

## 2.4 Relevance of nanotechnology in the health care system

As shown in WP 1 and 2, there are several areas with nanotechnological products in development and near commercialisation: 158 products are in an advanced development stage, 35 products on the market are enhanced by nanotechnology (Wagner, Zweck 2005). Farkas et al. 2004 used a bibliometric approach and searched the inno-

vation data base of the Institut für Gesundheits- und Sozialforschung (IGES) for nanomedicine innovations in the health sector. Both studies identified mostly identical fields of interest which are summarised in Table 2.7.

Table 2.7: Technological fields with nanotechnology relevance in the field of health care

<b>Fields as identified in this project (Wagner, Zweck 2005)</b>	<b>Fields as identified in the IGES innovation database</b>
Drug delivery systems	Drug delivery
Drugs and therapies	Combined (physical-pharmacological) therapies
	Predominantly physical therapy (e. g. hyperthermy, hypothermy, nuclear medicine etc.)
in vivo imaging	imaging, in vivo diagnostics
in vitro diagnostics	in vitro diagnostics
Implant materials	medical devices/implants
Active implants	Organ replacement, autologous material, tissue engineering
Cosmetics	not determined
not determined	medical aids (e. g. wheel chairs)
not determined	Protection from bioterrorism and natural disasters
not determined	Environmental toxicology, hygiene, occupational health, social medicine

In the IGES database 85 data sets were identified with the search term “nano\* for the above mentioned technological fields. However, most of the identified innovations were predominantly in an early developmental stage (basic research or preclinical research). Only 13 results could be related directly defined diseases. Six of them were innovations in the field of neoplasms (Farkas et al. 2004).

## **2.5 Effects of nanotechnological products**

### **2.5.1 Cardiovascular diseases**

The diagnostic group with the highest number of days of inpatient care in Germany is the group of cardiovascular diseases (Table 2.3). With 30 % of the projected total worldwide deaths it is the diagnostic group with a high relevance to public health.

As shown in chapter 2.3.3, Figure 2.4, stents and catheters are the cost drivers in therapy of cardiovascular diseases. Nanotechnologically modified stents could reduce the rate for restenosis. Currently radioactive and drug-coated stents are already in clinical use. Stents with nano-surface could not be detected so far. As drug coated stents show already significant improvements with respect to the rate of restenosis, Farkas et al (2004) do not expect a high substitution potential for nano-stents.

An in vivo sensor for the detection of creatine kinase and myoglobin was identified in the IGES innovation database. This sensor could allow the early detection of cardiac infarction and thus facilitate early lysis therapy. However, on the one hand this invention is in a very early stage of development (preclinical stage) and it is only a secondary preventive measure, i.e. the cause of the disease itself is not treated.

Due to these findings, Farkas et al (2004) do not expect any health economic impacts of nanotechnology in the cardiovascular field before 2010 because there are only few relevant innovations, which, in addition, are in a very early developmental stage.

It should be kept in mind, however, that due to the high number of patients with cardiovascular diseases, this is a segment of the health care system where even small cost effects (positive or negative ones) on a case basis will result in large cost impacts, if the whole affected population is taken into consideration.

## **2.5.2 Neoplasms**

Neoplasms contribute approximately 10 % of the total number of days of inpatient care (data for Germany) (Farkas et al. 2004) and require an average stay in hospital of 10 days in Europe (Table 2.4). Several nanotechnological products with relevance for cancer diagnostics and treatment could be identified. Among them are several diagnostic methods which allow an early detection of tumours and consecutively the genetic analysis of tumour cells could lead to personalized cancer therapy. Diagnostic microarrays are seen as an opportunity for efficient early diagnosis. However, they compete with various already established methods for early detection of cancer such as spectroscopic screening, cell biological and biochemical marker analysis. HTA of nanotechnologically assisted microarrays show some comparative advantages. However, further studies are necessary for a final evaluation (Ntzani und Ionnadis 2003). At present critical aspects are data analysis, reproducibility, cross-comparability, validation, and costs (Bucca et al. 2004).

Against the background of the ageing society, an overall increase of health care expenditure due to higher numbers of diagnostic procedures seems to be more likely than cost reductions unless nanotechnological diagnostic procedures are significantly

cheaper, more sensitive and more specific than established diagnostic procedures (Farkas et al. 2004).

Nanotechnological tumour therapeutics comprise ferrous nanoparticles for magnetic liquid hyperthermy and e. g. liposomal doxorubicin. The latter method is evaluated sceptically. As shown in the case study in more detail for liposomal doxorubicin (chapter 2.7) this therapeutic approach is not superior to the conventional therapy but more cost effective. With respect to therapeutic cancer interventions, Farkas et al. 2004 doubt that – from a systems perspective – significant cost savings will be possible even if nanomedical interventions were more cost-efficient than existing treatments because the number of patients will increase who survive their first tumour, and who will then suffer from a second tumour which also requires treatment.

### **2.5.3 Diseases of the nervous system**

In the diagnostic group of nervous disease no nanotechnological product has reached late stage of clinical studies. However, there are strong research activities. As many diseases in this area such as neurodegenerative diseases and muscle dystrophies can not be treated satisfactorily, new products could impact significantly the health system. Many patients with inflammatory brain disease are still young – a new therapy could lead to a significant reduction of required days of inpatient care.

### **2.5.4 Infectious diseases**

Currently, infectious diseases do not present a significant economic problem for the health system of industrialised countries. As the number of opportunistic infections rises due to the rising number of aggressive tumour therapies and transplantations (both are therapies that weaken the immune system), the spectrum of morbidity could change in the future. The same applies for fungal infections. A certain improvement of drug therapy can be expected as nano-encapsulated drugs could be applied site-directed and in higher concentrations. The case study of liposomal Amphotericin B will describe this in more detail (chapter 2.6). Also therapy for fungal keratomycoses could benefit from new drug formulations. However, there have been no detailed cost-effectiveness analyses of fungal keratitis (inflammation of the cornea) in the recent past (Ganegoda and Rao 2004). Microarrays for the detection of pathogens will play an increasing role. However, costs and limited sample throughput make it unlikely that planar microarrays will play a significant role in future pathogen detection schemes. Alternative microarray formats such as bead arrays may circumvent the cost and throughput limitations so that robust pathogen detection systems could be developed (Call 2005).

### **2.5.5 Musculoskeletal diseases, endoprostheses**

The model calculation 2 showed that this field will be the diagnose group with the highest health care costs due to high share of costs for personnel in care and physiotherapy but also for drugs and implants.

Nanotechnology-enhanced surfaces could improve lifespan of endoprostheses. Especially younger patients could benefit from this. However, in Germany only 12 % of all patients that undergo hip replacement belong to the group younger than 55 years<sup>19</sup>. Currently the costs of the implant average out at 950 €. This is only 15 % of the total costs (Farkas et al. 2004). Cost drivers are again personnel and infrastructure. Nanotechnologically improved implants could help to reduce health expenditures if they were significantly cheaper than other implants (small cost effects) or if they resulted in reduced inpatient care (significant cost effects).

## **2.6 Case study 1: Liposomal amphotericin B (AmBisome®)**

In the following chapters, health-economic impacts of nanotechnologies-enabled health innovations will be analysed in more depth for two case studies. The key criterion for the choice of these case studies was the availability of meaningful health economic data for a nanotechnologies-enabled health innovation.

Amphotericin B is an antifungal drug which is mainly used against fungal infections in transplant recipients, patients suffering from AIDS, or cancer patients. The major drawback of amphotericin B is its nephrotoxicity which can be overcome by liposomal delivery of the drug. Liposomal amphotericin B (AmBisome®) is a product of the US-based company Gilead Sciences.

Drug targeting is an efficient means to increase drug concentrations at the site of action and simultaneously reduce systemic adverse events. Liposomal drug delivery has several benefits. Liposomes are closed lipid spheres (1/1000th the width of a human hair) comprised of the basic components of natural human cell walls. By enclosing a drug in a liposome, it could be demonstrated improvements in the way a drug is released throughout the body and the amount of time it remains within the body. Liposomes may circulate in the bloodstream for extended periods, as compared to the same drug in a non-liposomal form. This may result in an extended treatment effect and a simplified dosing regimen for physicians and patients. In some cases, liposomal drugs have been

---

<sup>19</sup> It was not analysed in the study by Farkas et al. 2004 to which extent an increased life expectancy of old people would translate into an additional demand for endoprostheses with prolonged life-span.

shown to accumulate at the site of a tumour or infection delivering higher concentrations of the drug to a disease target. The liposome carrier is believed to play a role in reducing the harmful effects of certain drugs on healthy tissues, thereby offering the potential for an improved safety profile for certain drugs.

### **2.6.1 Clinical effectiveness**

In a study conducted by the Australasian Society for Infectious Diseases (ASID) (Sharon et al. 2002) the effectiveness of AmBisome<sup>®</sup> in comparison to conventional amphotericin was evaluated. In a randomized study of patients with cryptococcal meningitis AmBisome produced mycological eradication in 73 % of patients compared to 38 % with conventional amphotericin. AmBisome resulted in significantly earlier sterilization of cerebrospinal fluid than conventional amphotericin (7-14 days versus 21 days) and was less toxic. Hann and Prentice analysed the effectiveness of different lipid based amphotericin preparations (liposomal amphotericin, amphotericin B lipid complex, and amphotericin B colloidal dispersion). They found that doses of amphotericin B lipid preparations could be safely increased in serious fungal infections whereas the problems of nephrotoxicity and infusion related reactions such as chills, rigors, fevers and hypoxia could be reduced. There was also much less need for premedication, including steroids (Hann and Prentice 2001). Finally good properties of AmBisome in reducing proven emergent fungal infections, infusion-related toxicity and nephrotoxicity were demonstrated by a randomized double-blind comparative, multicentre trial (Cagnoni et al. 2000).

### **2.6.2 Cost-effectiveness**

In a clinical trial by Cagnoni et al. with persistently febrile neutropenic (drug induced destruction of certain blood cells) patients hospital costs from the time of first dose to discharge were significantly higher for all patients who received liposomal amphotericin B (€ 40,801 versus € 35,985) (Cagnoni et al. 2000). However, hospital costs were highly sensitive to the cost of study medication (€ 33,040 versus € 34,873 when drug costs were not included). Using decision analysis models and sensitivity analyses to vary the cost of study medications and the risk of nephrotoxicity, the break even-points for the cost of liposomal therapy were calculated to range from € 60 to € 73 per 50 mg for all patients and € 69 to € 93 per 50 mg in allogeneic bone marrow transplant patients. From this the authors concluded that the cost of liposomal amphotericin B and the patient risk for developing nephrotoxicity play a large role in determining whether liposomal amphotericin B is cost-effective as first-line empirical therapy in persistent febrile neutropenic patients (Cagnoni et al. 2000).

A randomized double-blind, placebo-controlled antifungal prophylaxis study of liver transplant recipients revealed that total costs for all antifungal drugs were the same in the two study groups. However, general prophylaxis against fungal infections with AmBisome was € 4,166 less expensive than treatment of proven invasive fungal infections among placebo patients (Tollemar et al. 1995).

In the case of three patients with a *Candida* vertebral osteomyelitis the therapy of two patients with liposomal amphotericin B resulted in reduced treatment times (Cone et al. 2004). The third person could be cured with non-liposomal amphotericin B.

In the case of a patient with cutaneous leishmaniasis (CL) which was resistant to traditional drugs a short course treatment of parenteral liposomal amphotericin B led to clinical cure with no side effects. The high cost of the drug was counterbalanced by easiest administration of the drug, reduction of hospitalization duration, absence of adverse side effects and a gain of comfort (Rapp et al. 2003). The authors conclude that for this patient the short course treatment with AmBisome proved to be suitable.

### 2.6.3 Barriers for the utilisation

The enormous costs<sup>20</sup> represent a high barrier for the prescription and utilisation of AmBisome (Sharon et al. 2002, Dupouy-Camet 2004). The high costs resulted in deliberately wrong information to patients. Sharon et al. illustrated that the benefit of reduced toxicity was denied to patients because of the high costs. Acceptable indication for the application of AmBisome is a failed therapy with conventional amphotericin B in the opinion of a group of Australian medical doctors (Sharon et al. 2002). In general this group thought that there was no difference between AmBisome and conventional amphotericin. This opinion was shared by several publications, especially as AmBisome competes not only with the conventional amphotericin B but also with innovative new active antifungal substances.

## 2.7 Case study 2: Pegylated liposomal doxorubicin hydrochloride

Most liposomal encapsulated drugs existed prior to their encapsulation as conventional therapeutic active substances. By encapsulation of the active substance in vesicular particles with a phospholipid bilayer, it is possible to alter pharmacological characteris-

---

<sup>20</sup> A standard therapy (3-6 weeks) against invasive aspergillosis in hemato-oncology with non liposomal amphotericin B costs € 107 to € 214. The same therapy with AmBisome® costs € 26,453- to € 52,906 (Dr. Claudia Wild, Institut für Technikfolgen-Abschätzung, Österreichische Akademie der Wissenschaften).

tics of a drug. Although drug targeting systems with nanoparticles and liposomal vesicles are the largest group among the patented nano-products only few studies were carried out under cost aspects. One example is pegylated liposomal doxorubicin. It is used as second-line therapeutic in the case of failure and resistance to platinum-containing regimen in ovarian carcinoma. Worldwide nearly 150 clinical studies were conducted dealing with cost effectiveness of this drug formulation. In a systematic review Forbes et al. analysed 143 studies (Forbes et al. 2002). The National Institute of Health and Clinical Excellence (NICE) published guidelines for the use of paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan for second-line or subsequent treatment of advanced ovarian cancer (Nice 2005).

### **2.7.1 Clinical effectiveness**

In the systematic review of Forbes et al. (2002) no significant differences in clinical effectiveness were reported between pegylated liposomal doxorubicin hydrochloride and topotecan, the former gold standard concerning overall survival, median survival, response rate, median time to response, median duration of response and quality of life (QoL). A new randomized phase III trial showed some improvement of quality of life and a survival advantage in platinum-sensitive patients (patients that can be treated with platinum as chemotherapeutic agent) (Thigpen et al. 2005). All studies showed significant differences in the incidence of adverse events. Topotecan was associated with increased haematological toxicities (including neutropenia, leukopenia, anaemia, and thrombocytopenia), alopecia (the status of having no hair), nausea and vomiting. Pegylated liposomal doxorubicin hydrochloride increased the incidence of palmar-plantar erythrodysesthesia, stomatitis, mucous membrane disorders and skin rashes (Forbes et al. 2002). Thigpen et al. reported results from prospective and retrospective studies that demonstrated the improved cardiac safety of pegylated liposomal doxorubicin compared to conventional anthracyclines (Thigpen et al. 2005).

### **2.7.2 Cost-effectiveness**

The cost analysis in different countries revealed cost saving potential by therapy with pegylated liposomal doxorubicin in comparison to topotecan. Ojeda et al. (2003) reported a cost saving of 2,209 € for Spain (total costs 9,614 € with pegylated liposomal doxorubicin versus 11,824 € with topotecan), Capri et al. (2003) reported a cost saving of 6,979 € for Italy (total mean costs 8,812 € with pegylated liposomal doxorubicin versus 15,788 € with topotecan). In both cases the higher acquisition cost of pegylated liposomal doxorubicin offset the higher costs of managing the adverse events related to treatment with topotecan. Further analysis showed that when a full probabilistic cost-effectiveness analysis was undertaken and effectiveness expressed in terms of mean

survival duration, there was a high probability that pegylated liposomal doxorubicin is more cost effective (70-80 %). However, the possible differences in health-related quality of life (HRQoL) between the two therapies, reflecting the differences in adverse events, may produce quite different cost-effectiveness results when effectiveness is expressed in terms of quality-adjusted life-years (QALYs) – a preferable measure when both length of life and quality of life (QoL) are potentially influenced. Therefore, although pegylated liposomal doxorubicin is very likely to have lower costs than topotecan, its overall cost-effectiveness is unclear (Forbes et al. 2002).

### **2.7.3 Barriers for the utilisation**

Currently, most trials do not show significant improvement in clinical effectiveness in the main clinical outcomes (Forbes et al. 2002). Thus pegylated liposomal doxorubicin is recommended by the NICE only as second-line agent for the treatment of women with relapsed or refractory disease (Johnston 2004). The high price is a barrier for its utilisation. As long as pegylated liposomal doxorubicin costs 20 times more than standard doxorubicin in France the standard form is postulated to be suitable for most patients as long as cardiac function is closely monitored (Anonymous 2004). However, future clinical trials could further define and maximize the role of pegylated liposomal doxorubicin in the treatment of ovarian cancer and other gynaecologic malignancies (Thigpen et al. 2005).

## **2.8 Conclusions**

In the past, health innovations were mainly assessed with respect to efficacy and improved quality of life, whereas cost considerations were not of prominent importance. Nowadays, the situation has changed: health care costs do matter – for various reasons:

On the one hand, national health expenditures will increase significantly if the current practice is also pursued in the future: while EU-15 member states spent 6.2 % of their Gross Domestic Product on health care in 2002, this share is likely to rise to 8.9 % in 2050 (chapter 2.3.2). The main drivers are demographic changes, leading to an ageing society, due to decreasing birth rates and increasing life expectancy, and medical innovations which alter the patterns of the most prevalent diseases (increase of complex and chronic diseases), and which offer new diagnostic and therapeutic options for higher quality of life and higher quality of care, but often also at higher costs.

The changing age structure of the society together with an increase in health care expenditure challenges the sustainability of the health care systems, because most of

these systems are based on a pay-as-you-go financing mode. Because of this mode, population ageing unbalances the relation between health care expenditures and health care contributions, because fewer people of working age will have to support those in retirement. This is reflected by the indicator of old-age dependency, which is expected to rise in EU-15 from 24.1 in 2000 to 47.2 in 2050.

Therefore, present health care systems will no longer be affordable in the medium to long term and require significant changes for which several options can be taken into consideration, among them

- Structural reforms (e. g. change financing mode of health care systems, reduced coverage, reduce institutional inefficiencies in health care delivery),
- Investments into the health of the population,
- Main cost drivers as priority targets for cost reductions.

With respect to health innovations, it can be concluded that efficacy and improved quality of life will remain a necessary prerequisite, but will no longer be sufficient. In addition, health innovations will increasingly be assessed with respect to the costs at which the improvements come.

Against this background, it was the aim of this chapter to assess

- what the possible impact of nanomedical innovations on future health care costs might be, i. e., to which extent nanomedical innovations bear the potential of increasing or decreasing health care costs,
- what their competitiveness with respect to established products, procedures or interventions may be.

Based on model calculations performed by Farkas et al. 2004 for Germany, major drivers for future health care costs were identified: In addition to demographic changes, these are major cost-causing diseases (cardiovascular diseases, diseases of the nervous system, musculoskeletal diseases, and neoplasms) and personnel-intensive care (e. g. days in hospital). From this, it could be concluded that nanomedical innovations are likely to have a positive impact on future health care costs by reducing them if they

- aim at major cost-causing diseases, such as cardiovascular diseases, diseases of the nervous system, musculoskeletal diseases, and neoplasms,
- reduce personnel costs, e. g. by reducing the required days of inpatient care, for a given disease,
- contribute to "healthy ageing", i. e. in raising the health status of the population.

On the other hand, nanomedical innovations are likely to increase future health care costs if they

- come as add-on technology, which offer a measurable, but only small health effect at significant costs, so that the cost-benefit-ratio is unfavourable,
- aim at diseases of minor cost relevance (e. g. infections, diseases with low prevalence and incidence),
- induce additional procedures without substantial health effect (e. g. earlier or more frequent diagnosis).

In the chapters 2.4 and 2.5, it was analysed to which extent the currently foreseeable nanomedical innovations fit into the general considerations outlined above. The analysis of nanotechnological innovations has shown that 158 products are in an advanced development stage, 35 products on the market are enhanced by nanotechnology. Due to few products in the clinic, and most of them in the R&D pipeline, it is expected that until 2010, nanotechnology will not significantly impact the health care costs.

According to the study of Farkas et al 2004, and supported by the views of the responding European experts in our survey (see chapters 2.2.2, 4.2) relevant fields for the evaluation of effects of nanotechnology cost drivers in the health system will be the major disease groups cardiovascular disease, neoplasms, diseases of the nervous system and musculo-skeletal diseases. For all groups technology dependent costs account for a maximum of 20 % of the total costs. Thus nanotechnological innovations can have a significant impact on health costs if they reduce personnel costs by reduction of the number of days in hospital. Other savings may occur in ambulatory care costs, i.e. for diagnostic tests and for some pharmaceutical therapies.

In detail nanotechnology is likely to impact future health expenditures as follows:

- Cardiovascular disease (including stroke) and neurodegenerative disease do not show significant potential for cost reduction through nanotechnologies. Cost drivers in this disease groups are intensive care for chronic patients and rehabilitation of stroke patients. Some cost reduction seems to be possible in diagnostic tests.
- Neoplasms show a certain potential for some cost savings by early screening and prevention. On the other hand, add-on innovations of conventional chemotherapeutic drugs. i. e. new drug formulations which improve the efficacy of conventional drugs, are likely to come at higher drug costs whereas it remains to be seen whether the overall case costs can be reduced (e. g. by shorter stay in hospital, fewer complications). Another consequence, which again could result in higher health care expenditure from a systems perspective, could be that an increasing share of tumour patients survive their first tumour, but require additional treatments due to the occurrence of secondary tumours.
- Infectious disease could undergo a certain improvement of drug therapy as nano-encapsulated drugs could be applied site-directed and in higher concentrations.

- Musculoskeletal diseases are the group with expected small effect, as prosthesis with longer durability do not play an important role for the (mainly older) recipients of endoprostheses. Moreover medicinal products and implants account for only 15 % of the total costs. Nanotechnological products will only have the potential to reduce health expenditures if they reduce the number of days of inpatient care.

Significant impetus for innovation activities is expected from the development of combined therapeutic approaches (i.e. combination of diagnosis and therapy) which will lead to personalized medicine. Still, apart from the technological improvement future framework for approval and reimbursement are key issues for the economic impact of nanotechnology on the health care system. The extent to which innovative technologies are added to the list of reimbursement by insurances or the national health system is a political question – facing the financial shortage in the health system prices and cost-effectiveness ratios will be very crucial. Only cost efficient health technologies are likely to be reimbursed. This is a change to foster also process innovations that help to reduce costs in the health system.

Despite significant efforts to identify case studies which allow the analysis of costs of nanotechnological products in more detail, only few studies could be found at all. A broader set of health economic data was only available for two case studies, liposomal amphotericin B and pegylated liposomal doxorubicin hydrochloride, presented in chapters 2.6 and 2.7. Liposomal amphotericin B is an example for a conventional drug whose profile of side effects (nephrotoxicity) can be positively changed due to liposomal drug delivery. However, the additional positive health effect of reduced nephrotoxicity comes at prohibitively high costs, which has up to now prevented liposomal amphotericin C from being used more broadly than in exceptional cases. Competitiveness with conventional amphotericin B can only be expected if the cost-effectiveness can be substantially improved. The case is different for pegylated liposomal doxorubicin hydrochloride. It shows a similar or even better effectiveness than the current gold standard topotecan, but shows a different pattern of adverse effects. Although there is a high probability that treatment with pegylated doxorubicin is cheaper than conventional treatments due to lower treatment costs for adverse effects, the overall cost-effectiveness has not yet been convincingly established. From these few studies it cannot yet be concluded whether and which nanotechnologically derived therapies will be more cost efficient than conventional therapies.

## 2.9 References

Anonymous (2004): Doxorubicin liposomal pegylated: new preparation. Breast cancer: not just a question of short-term cardiac effects. *Prescrire Int.* 13 (71), pp. 90-91

- Bucca, G.; Carruba, G., Saetta, A.; Muti, P.; Catagnetta, L.; Smith, C.P. (2004): Gene expression profiling of human cancers. *Ann N Y Acad Sci*; 1028, pp. 28-37
- Brockmann, H. (2002): Why is less money spent on health care for the elderly than for the rest of the population? Health care rationing in German hospitals. *Soc Sci Med* 55 (4), pp. 593-608
- Cagnoni, P.J.; Walsh, T.J.; Prendergast, M.M. Bodensteiner, D.; Hiemez, S.; Greenberg, R.N. Arndt, C.A.; Schuster, M.; Seibel, N.; Yeldandi, V.; Tong, K.B. (2000): Pharmaco-economic analysis of liposomal amphotericin B versus conventional amphotericin B in the empirical treatment of persistently febrile neutropenic patients. *J Clin Oncol* 2000, 18(12), pp. 2476-2483
- Call, D.R. (2005): Challenges and opportunities for pathogen detection using DNA microarrays. *Crit Rev Microbiol*, 31(2), pp. 91-99
- Capri, S.; Cattaneo, G. (2003): Cost-minimization analysis of pegylated liposomal doxorubicin versus topotecan for the treatment of ovarian cancer in Italy. *Clin Ther* 25(6), pp. 1826-1845
- Cone, L.A.; Byrd, R.G.; Potts, B.E.; Wuesthoff, M. (2004): Diagnosis and treatment of Candida vertebral osteomyelitis. Clinical experience with a short course therapy of amphotericin B lipid complex. *Surg Neurol* 62(3), pp. 234-237
- Dubouy-Camet, J. (2004): New drugs for the treatment of human parasitic protozoa. *Parasitologia* 24 (1-2), pp. 81-84
- European Commission (2005): Hospital Discharges of in-patients by diagnosis - average length of stay. [http://europa.eu.int/comm/health/ph\\_information/dissemination/echi/echi\\_22\\_en.pdf](http://europa.eu.int/comm/health/ph_information/dissemination/echi/echi_22_en.pdf)
- Farkas, R.; Monfeld, C.; Schmitz-Rode, T.; et al. (2004): Nanotechnologie pro Gesundheit: Chancen und Risiken. Bericht im Auftrag des BMBF. [www.bmbf.de/pub/nano\\_pro\\_gesundheit\\_bericht.pdf](http://www.bmbf.de/pub/nano_pro_gesundheit_bericht.pdf)
- Forbes, C.; Wilby, J.; Richardson, G.; Sculpher, M.; Mather, L.; Reimsma, R. (2002): A systematic review and economic evaluation of pegylated liposomal doxorubicin hydrochloride for ovarian cancer. *Health Technol Assess* 6(23), pp. 1- 130
- Ganegoda, N.; Rao, S.K. (2004): Antifungal therapy for keratomycoses. *Expert Opin. Pharmacother.* 5(4); pp. 865-874
- Hann, I.M.; Prentice, H.G. (2001): Lipid-based amphotericin B: a review of the last 10 years of use. *Int J Antimicrob Agents*, 17(3), pp. 161-169

- Nice 2005: Paclitaxel, pegylated liposomal doxorubicin hydrochloride and topotecan for second-line or subsequent treatment of advanced ovarian cancer. Review of Technology Appraisal Guidance 28, 45 and 55
- Ntzani, E.E.; Ioannidis, J.P.A. (2003): Predictive ability of DNA microarrays for cancer outcomes and correlates: an empirical assessment. *Lancet*, 362, (November 1), pp. 1439-44.
- Johnston, S.R. (2004): Ovarian cancer: review of the National Institute for Clinical Excellence (NICE) guidance recommendations. *Cancer Invest.* 22(5), pp. 730-742
- OECD (2002): Working together towards sustainable development. The OECD experience. Paris, France: OECD publication service.
- Ojeda, B.; de Sande, L.M.; Casado, A.; Merino, P.; Casado, M.A. (2003): Cost-minimisation analysis of pegylated liposomal doxorubicin hydrochloride versus topotecan for the treatment of patients with recurrent epithelial ovarian cancer in Spain. *Br J Cancer*, 89(6), pp. 1002-1007
- Rapp, C.; Imbert, P.; Darie, H.; Simon, F.; Gros, P.; Debord, T.; Roue, R. (2003): Liposomal amphotericin B treatment of cutaneous leishmaniasis contracted in Djibouti and resistant to meglumine antimonate. *Bull Soc Pathol Exot* 96(3), 209-211
- Sharon, C.A.; Chen S.C.; Australasian Society for Infectious Diseases (ASID) Mycosis Interest Group (2002): Cryptococcosis in Australasia and the treatment of cryptococcal and other fungal infections with liposomal amphotericin B. *J Antimicrob Chemother* 40 (Suppl 1), pp. 57-61
- Siebert, U. (2005): Entscheidungsanalytische Modelle zur Sicherung der Übertragbarkeit internationaler Evidenz von HTA auf den Kontext des deutschen Gesundheitssystems. DAHTA@DIMDI. ISBN 3-89906-739-8
- Surcke, M.; McKee, M.; Sauto Arce, R.; Tsoleva, S.; Mortensen, J. (2005): The contribution of health to the economy in the European Union. Luxembourg: Office for Official Publications of the European Communities, 2005, ISBN 92-894-9829-3
- Thigpen, J.T.; Aghajanian, C.A.; Alberts, D.S.; Campos, S.M.; Gordon, A.N.; Markman, M.; McMeekin, D.S.; Monk, B.J.; Rose, P.G. (2005): Role of pegylated liposomal doxorubicin in ovarian cancer. *Gynecol Oncol.* 96(1), pp. 10-18
- Tollema, J.; Höckerstedt, K.; Ericzon, B.-G.; Jalanko, H.; Rindgén, O. (1995): Liposomal amphotericin B prevents invasive fungal infections in liver transplant recipients. *Transplantation*, 59(1), pp. 45-50

Wagner, V.; Zweck, A. (2005): Nanobiotechnology in the medical sector - Drivers for development and possible impacts. Confidential report for WP1 (Current status of nanobiotechnology for medical applications in Europe) and WP2 (Identification of the main drivers and challenges for medicinal nanobiotechnology and its impact on the medical sector), Düsseldorf: Zukünftige Technologien Consulting.

Zweifel, P. (2003): Medical Innovation: A challenge to society and insurance. The Geneva Papers on Risk and Insurance. 28(2), pp. 194-202

## **3 Social and ethical issues in nanobiotechnology in the medical sector**

### **3.1 Introduction**

The necessity to address social and ethical issues of nanotechnologies in addition to scientific, economic and political issues (as analysed by Wagner, Zweck 2005) has been widely recognised, as reflected e. g. in the Communication from the European Commission "Towards a European Strategy for Nanotechnology"<sup>21</sup> and the Action Plan "Nanosciences and nanotechnologies: An action plan for Europe 2005-2009"<sup>22</sup>.

Nanotechnologies have also been identified as challenging new ethical issues for the coming decade by the European Group on Ethics in Science and New Technologies to the European Commission<sup>23</sup>, and the international Nordic Committee on Bioethics<sup>24</sup>. Ethical issues of nanotechnologies are on the agenda at the French Comité consultatif national d'éthique pour les sciences de la vie et de la santé (CCNE)<sup>25</sup> and Italy's National Bioethics Committee, as well as in Canada by the Science and Technology Ethics Committee (CEST) in Quebec, Canada<sup>26</sup>. The CEST has announced a preliminary report on the subject and a public forum for autumn 2005, and a position statement for spring 2006<sup>27</sup>.

This reflects on the one hand the intention to avoid mistakes that have been made with other technologies, such as biotechnology and genetic engineering (see e. g. Fisher 2005; Toumey 2004; Mehta 2004; Einsiedel, Goldenberg 2004; Matsuura 2004). On the other hand, it reflects the notion that science and technology only exist in a social context, and that we cannot understand how science and technology develop without understanding both the social conditions that produce them and the social impacts of science and technology on society. A better understanding of the interaction and mutual interdependence of science, technology and society could lead to more informed

---

21 COM(2004) 338; [ftp://ftp.cordis.lu/pub/nanotechnology/docs/nano\\_com\\_en.pdf](ftp://ftp.cordis.lu/pub/nanotechnology/docs/nano_com_en.pdf)

22 COM(2005) 243; [ftp://ftp.cordis.lu/pub/nanotechnology/docs/nano\\_action\\_plan2005\\_en.pdf](ftp://ftp.cordis.lu/pub/nanotechnology/docs/nano_action_plan2005_en.pdf)

23 see EGE-Newsletter "Ethically speaking" No.5, p. 5;  
[http://europa.eu.int/comm/european\\_group\\_ethics/docs/issue5.pdf](http://europa.eu.int/comm/european_group_ethics/docs/issue5.pdf)

24 Result of the Think tank "Bioprophecy - the future of ethics and biotechnology", 25-26 November 2004 in Denmark; <http://www.ncbio.org/bioprofetier.pdf>

25 <http://www.ccne-ethique.fr>

26 <http://www.ethique.gouv.qc.ca>

27 see EGE-Newsletter "Ethically speaking" No.5, p. 21;  
[http://europa.eu.int/comm/european\\_group\\_ethics/docs/issue5.pdf](http://europa.eu.int/comm/european_group_ethics/docs/issue5.pdf)

decisions about how to invest in science and technology, when and how to (not) regulate technological development, how to address ethical challenges etc (Lewenstein 2005; Macnaghten et al. 2005). As a consequence, ethical and sociological reflection should not be considered as an "add-on" which follows scientific-technological research and development, but rather accompany it as an integral part (Schummer 2004).

In the following chapters, we will give an overview of the social and ethical issues of nanotechnologies with specific reference to biomedical applications which are presently being discussed. However, there are several difficulties and limitations to it:

- Despite several reports and publications, the scientific investigation of social and ethical issues of nanotechnologies is just emerging and not yet well developed.
- In addition, the topic in itself is difficult to deal with for the following reasons:
  - Nanotechnologies is an umbrella term for manipulations at the atomic level, involving a broad range of disciplines and having a multitude of possible products, services and applications. In addition to this large diversity, nanotechnologies are at the same time at an early stage of development: first applications are just emerging, while most applications are still hypothetical with considerable uncertainty whether, when and how they will (ever) become realised and what the contexts of their application might be: some currently envisioned applications of nanotechnologies may never be realised on a significant scale, while unanticipated scientific breakthroughs or societal demands may lead to applications that are currently not foreseen (The Royal Society & The Royal Academy of Engineering 2004, p. 51).
  - This makes a specific analysis of ethical and social issues difficult, because it is not clear which developments should be covered in the analysis, and into which contexts the analysed developments should be embedded.
- Nevertheless, some, albeit few and preliminary research has taken place: Several recent reports have addressed these social and ethical issues, among them Paschen et al. 2003; The Royal Society & The Royal Academy of Engineering 2004; Malsch et al. 2004; Wood et al. 2005; Türk et al. 2005a; Türk et al. 2005b, and many articles have been published (e. g. Roco 2003a; Mnyusiwalla et al. 2003; Sweeney et al. 2003; Weil 2003; Sheremeta, Daar 2004; Dunkley 2004; Berne 2004b; Berne 2004a; Baber 2004; Lopez 2004; Baird, Vogt 2004; Laurent, Petit 2005; Grunwald 2005; Invernizzi, Foladori 2005 to name but a few). However, these analyses relate to the whole field of nanotechnologies rather than to selected subfields. Due to the early stage of the whole field, these are mainly basic and general deliberations, and are therefore often not highly specific for nanotechnologies, but rather valid for emerging technologies with a certain potential.
- A more differentiated analysis of social and ethical issues in subfields of nanotechnologies, e. g. medicine, is only beginning. Therefore, there are only few publications which specifically deal with social and ethical issues of medical applications of

nanotechnologies (see e.g. Baumgartner et al. 2003; Sheremeta 2004; Baumgartner 2004; Türk et al. 2005a).

- Issues raised by nanotechnologies applications have, in part, been dealt with in depth in other technological contexts, so that the analysis of ethical and social issues of nanotechnologies can establish links with this work (MacDonald 2004). For example, nanotechnologies-enabled diagnostics may have close links with aspects of genetic testing. But even if the ethical and social issues are not genuinely new or exclusively specific for nanotechnologies, this does not render them less valid. Rather, due to the enabling nature of nanotechnology some issues may become (even) more critical, and there may be shifts in emphasis. In addition, new and specific issues may arise (Baumgartner 2004). Moreover, many potential applications and visions explicitly refer to the convergence of nanotechnologies, biotechnology, ICT and cognitive sciences (National Science Foundation 2002; Roco 2003b), which seems to be a specific feature of the nanotechnologies discourse (see chapter 3.12.1).

In the following chapters, we will give an overview of the social and ethical issues of nanotechnologies with specific reference to biomedical applications which are presently being discussed, and which were derived from an analysis of recent publications as well as from interviews.

## **3.2 Human health impacts**

### **3.2.1 Introduction**

The expectation that nanotechnological applications in medicine will lead to positive health impacts for individual patients as well as the public is a major driving force for this field, and also characterises the prevailing view in the general public (see chapter 3.12). Health benefits from nanotechnologies have extensively been addressed in the WP 1 and 2-report of this project (Wagner, Zweck 2005) and will be summarised shortly in chapter 3.2.2. However, possible health benefits must be carefully balanced against possible adverse health effects. An overview of health risks will be given in chapter 3.2.3 and more detailed information on health risks related to nanoparticles in chapter 3.4. In addition, broader use of nanotechnological applications in medicine will have impacts on the structure and organisation of health care delivery which will be outlined in chapter 3.2.4. Possible cost impacts have been addressed in chapter 2. Finally, the question will be addressed what the relevant prerequisites and frame conditions are to realise health benefits and minimise health risks (chapter 3.2.5).

### 3.2.2 Health benefits from nanotechnological applications in medicine

Health benefits from nanotechnologies have extensively been addressed in the WP 1 and 2-report of this project (Wagner, Zweck 2005), as well as by Paschen et al. 2003; Baumgartner et al. 2003; Bogedahl et al. 2003 and Farkas et al. 2004, with the following key findings:

- *Biomedical and pharmaceutical research.* Nanotechnologies are expected to contribute to biomedical research, leading to a better understanding of mechanisms and causes of disease, and to pharmaceutical drug discovery and development (Jain 2005).
- *Diagnostics.* In the field of diagnostics, the optimisation of existing diagnostic procedures is expected, as well as the development of new diagnostic tools. With the help of nanotechnologies, the quality of diagnostic procedures is expected to increase with respect to sensitivity, specificity and the range of testable functions and states. Moreover, nanotechnologies-derived diagnostics will not only be available to specialists, but certain forms (e. g. lab-on-a-chip) will also be available to e. g. general practitioners or even the patient himself, and will also enable point-of-care diagnostics. Certain diagnostic procedures will become quicker, making high-throughput analysis and screening possible, will be performed earlier in the disease course, will be performed more often in order to monitor the development of risk factors or the progression of disease, and even permanent surveillance and real-time monitoring of risk patients is possible.
- *Therapeutic interventions.* Nanotechnologies are expected to contribute to the optimisation of existing therapies by making the interventions less invasive, by developing more specific treatments with fewer side-effects and higher effectiveness, and by providing more causal than symptomatic treatments. Moreover, the development of new therapeutic principles is expected, the development of treatments for previously untreatable or incurable diseases, the improved compensation of disabilities and impaired functions, and the provision of alternatives to ethically problematic biomedical procedures (such as fetal cell transplantation or therapies based on human embryonic stem cells, organ donation and transplantation, xenotransplantation (see e. g. Hüsing, Schicktanz 2000; Hüsing et al. 2001; Hüsing et al. 2003).
- *Theranostics.* It is the aim to integrate diagnosis and therapeutic intervention into one procedure, termed theranostics. If, e. g. a tumour is detected by medical imaging, it should become possible to remove or treat it immediately. In this way, the number of subsequent interventions performed on one patient should be minimized.

It is expected that the new and improved diagnostic procedures and therapeutic interventions outlined above will result in

- improved quality of health care,
- a higher proportion of intervention and prevention in very early stages of diseases before symptoms become clinically manifest, instead of treating chronic diseases,
- improved quality of life, and
- a prolonged life span, but also an increase in healthy life years<sup>28</sup>.

### 3.2.3 Health risks from nanotechnological applications in medicine

The present discussion about possible health risks emanating from nanotechnologies focus on the biological effects of nanoparticles. This issue will be dealt with in detail in chapter 3.4. Also related, but not restricted to possible health risks due to nanoparticles are health risks due to

- *Substandard quality, safety and efficacy.* In the EU, medicinal products and medical devices are not allowed to enter the market unless their compliance with regulatory requirements has been shown convincingly. For medical devices, the regulatory requirements are laid down in the three European Directives 93/42/EEC (Medical Devices Directive), 90/385/EEC (Active Implantable Medical Devices Directive) and 98/79/EC (In Vitro Diagnostic Directive). For medicinal products, the directives 2001/83/EC (Medicinal Products for Human Use) and 2001/20/EC (Clinical Trials on Medicinal Products for Human Use) apply. These regulations do not apply to cosmetics. Although it is the purpose of these directives to ensure that only those products enter the market which are of sufficient quality, safety and efficacy, it may be challenging to carry out this assessment in practice, because the required knowledge about the behaviour and biological effects of nanoparticles is presently too patchy and assessment schemes are not specifically tailored to assess nanoparticle-specific questions and require amendment (SCENIHR 2005; chapter 3.4; chapter 3.7) in order to take the specificities of nanotechnologies into account appropriately.

In addition, the regulatory requirements and assessment schemes differ, depending on whether a product is classified as a medical device, a medicinal product, or a cosmetic. For safety and quality reasons, it is therefore of high importance that

---

<sup>28</sup> Healthy life years (HLY) is a health expectancy indicator which combines information on mortality and morbidity. The data required are the age-specific prevalence (proportions) of the population in healthy and unhealthy conditions and age-specific mortality information. A healthy condition is defined by the absence of limitations in functioning/disability. The indicator is calculated separately for males and females. The indicator is also called disability-free life expectancy (DFLE).

products are subjected to the appropriate regulation and assessment schemes. However, it is expected that more "borderline" products will result from the application of nanotechnologies for medical applications. These "borderline" products will be difficult to classify because they do not unambiguously fall into the definitions given by the directives mentioned above<sup>29</sup> (Paschen et al. 2003) so that a "clearing-house mechanism" and, eventually, an amendment of the regulations, will be required in the medium term. Regulatory expertise in nanotechnologies is of major importance to deal with these challenges and strike an appropriate balance between ensuring health, safety and quality and at the same time make innovation and commercialisation of nanotechnologies derived products possible.

- *Side and adverse effects.* The above-mentioned regulations, but also principles of biomedical ethics require a careful balancing of the benefits of a medical intervention or diagnostic procedure with the risks, not only when placing such products on the market, but also in the research phase. A careful balancing of benefits and risks is especially important, because not all risks may be known or deducible from existing therapies. Moreover, it cannot be ruled out that medical interventions based on nanotechnologies could have unprecedented biological and adverse effects, which have not been encountered before due to the novelty of these interventions. This is especially true due to the lack of knowledge regarding the behaviour of nanoparticles in the human body, due to the inherent properties of some drug delivery systems to move across biological barriers, if new therapeutic principles are to be established (e. g. gene therapy), and if complex systems which e. g. comprise biological, nanotechnological and IT components and/or for which not all relevant parameters of safety and quality can reasonably be tested beforehand (e. g. long-term effects, interference with other components or systems).
- *Balancing of patients interests against scientific and commercial interests.* In addition to the above-mentioned uncertainties in our knowledge of certain risks, the striving for scientific reputation or commercial interests could also pose challenges to a risk-benefit assessment on the basis of the principles of medical ethics of non-maleficence and duty of beneficence.

### 3.2.4 Changes in health care delivery

Several changes in health care delivery can be expected from the scientific-technological developments outlined in chapter 3.2.2:

- *Personalised medicine.* By providing diagnostic systems (e. g. for screening), nanotechnologies will be an enabler for extended risk specifications on the level of

---

<sup>29</sup> An example are human tissue engineered products which are neither covered by the medicinal products nor the medical device directives in their present form. Therefore, an amendment of the medicinal products directive by a regulation for advanced therapies has been proposed; for details see <http://pharmacos.eudra.org/F2/advtherapies/index.htm#pb> and Hüsing et al. 2004b

the individual, which may open up the possibility to adopt preventive risk management strategies and to choose the most appropriate intervention for the affected individual. Therapeutic interventions (e. g. dosing of drugs) could be tailored to the individual response, if nanotechnologies-enabled monitoring of disease progression and monitoring of effects of therapeutic interventions could be applied. This trend towards personalised medicine could increase the available options for patients to exert more self-determination and self-responsibility on their health, but on the other hand this option may also turn into a duty. The question to which extent patients wish to and are able to use these options for their benefit is discussed in chapter 3.2.5.

- *Convergence with ambient intelligence.* The application of nanotechnologies will support the introduction of telemedicine into health care delivery; on the one hand through nanotechnologies-enabled devices such as sensors which include ICT components. On the other hand, these devices will increasingly be interconnected, leading to a convergence of telemedicine/e-health with ambient intelligence. This will not only require an appropriate ICT infrastructure. It will also lead to changes in work and information flow in health care, and in the tasks that have to be performed by medical staff.
- *Shift of (chronic) diseases to older age.* Earlier diagnosis and risk specification before clinical symptoms become manifest, coupled with preventive measures and improved therapies are expected to shift chronic disease states to older age. This, on the one hand, should allow a higher quality of life until older age, but could on the other hand have significant impacts on demographic development, and the need for social support systems for the elderly. If treatments for those diseases improve which formerly led to death at young age (e. g. cystic fibrosis, phenylketonury), but the disease cannot be cured or the defects remedied, then there will be an increasing need for research and specific care concepts how adults with these diseases can be treated appropriately.
- *"Exchange of spare parts".* Nanotechnologies are seen as an enabler for the provision of interventions which compensate disabilities and impaired motor, sensory and cognitive functions. This could lead to a notion of medicine as providing "spare parts" which are exchanged in case of disease or accident in order to "repair" defects, with significant impacts on the role of the body for personal identity (see also chapter 3.10), and also on our understanding of health and disease.

### **3.2.5 Prerequisites and frame conditions for realising health benefits and minimising health risks**

Whether health benefits of nanotechnologies can be realised and associated health risks minimised, depends to a large extent on the frame conditions under which the development, commercialisation and clinical use of nanotechnologies for biomedical applications takes place.

- *R&D*. In order to ensure that only products and services with proven safety, quality, effectiveness and efficacy are brought to the clinic, high quality preclinical and clinical research is required. Moreover, frame conditions should be such that a premature "rush to the clinic" can be effectively prevented and that general ethical principles are respected (e. g. respect for free and informed consent, respect for vulnerable persons, respect for privacy and confidentiality, respect for justice and inclusiveness, balancing benefits and harms, minimizing harm, maximising benefit) (Sheremeta 2004).
- *Market approval*. As outlined in chapter 3.2.3, the present EU regulations for market approval of medical devices, medicinal products and cosmetics do not take the specific health risks emanating from nanoparticles sufficiently into account in the existing assessment schemes. Related research needs, needs for the development of test systems and needs for amendments of regulation have been identified by SCENIHR 2005 (see also chapter 3.4).

Moreover, "borderline products" which do neither clearly fall into the scope of the medicinal products nor the medical devices regulation are known from the field of tissue engineering (Hüsing et al. 2004a; Bock et al. 2005). Today, nanotechnology is being applied to develop scaffolds for human tissue engineered products with the aim to improve scaffolds customised for specific tissue growth (Wagner, Zweck 2005, chapter 10). In the nutrition field, functional food products also fall between food and medicinal products regulations (Hüsing et al. 1999; Menrad et al. 2000), and nanotechnology drug delivery systems or nanoparticulate nutrient preparations are also applied for improved nutrient or functional ingredient delivery in functional foods. Against this background, "clearing house mechanisms" in regulatory authorities may be required in order to properly deal with such "borderline products" and which may involve nanotechnologies in their manufacturing. However, the "borderline character" is inherent to these specific products, but is not specifically conveyed to them by nanotechnologies. Nevertheless, nanotechnologies expertise in regulatory authorities is of major importance to deal with these challenges and strike an appropriate balance between ensuring health, safety and quality and at the same time make innovation and commercialisation of nanotechnologies-derived products possible.

The latter is an important prerequisite for the realisation of possible health benefits of nanotechnologies-derived products and services which depends on their availability and commercial viability on the market. The higher the requirements to prove safety, quality, efficacy, and – possibly also superiority over existing products and services in terms of costs or quality of life gains – the higher the barriers are for innovative products and services, especially if they are targeted at a relatively small patient population (rare diseases, orphan drugs), are developed by relatively resource-poor SMEs, or show superiority only in difficult to prove characteristics, such as long-term effects (e. g. avoidance of frequent relapse) or cost savings related with different cost distributions. In the regulatory approval of medicinal products, provisions are established to reduce these barriers, e. g. the orphan drug regulation,

possibilities for reduced fees for SMEs, or conditional approvals. The performance and appropriateness of these provisions should be evaluated regularly, also with respect to nanotechnologies.

- *Clinical availability.* Of major importance are the conditions under which patients who could benefit from nanotechnologies-enabled products and services have access to them. In most health care systems, reimbursement by statutory and private health insurances will function as a gate-keeper. Given the fact that most nanotechnologies-enabled products and services will not come at lower costs than their conventional counterparts with which they compete (see chapter 2), there is an urgent need for transparency in these resource allocation decisions in health care and that the decisions are made on a well-informed basis. Health economic assessments should play an important role in these decisions. In addition, information and education of patients as well as enabling them to take self-responsibility for their health is important.
- *Quality assurance during use.* Quality assurance during use strongly contributes to the realisation of health benefits and the avoidance of unintended impacts. This comprises
  - Vigilance systems by which faulty medical devices or adverse effects of medicinal products can be discovered and tracked,
  - Education, qualification and information of medical staff, but also of patients,
  - Certification, if applicable, of institutions offering certain services (e. g. genetic testing) (Ibarreta et al. 2004),
  - Health technology assessments and guidelines for the improvement of medical care and for supporting the choice of the most appropriate intervention, and
  - Using the products and devices only in defined and appropriate contexts (e. g. for medical purposes, with sufficient counselling).

### 3.3 Environmental impacts

Nanotechnologies have basic characteristics from which both possible positive environmental impacts as well as negative ones can be deduced (Table 3.1). In general, the environmental impacts of nanotechnologies for biomedical applications are thought to be lower than for other application areas, e. g. energy conversion or materials. Nevertheless, several issues require consideration, with risks from nanoparticles (for details see chapter 3.4) being the most prominent ones.

Table 3.1: Possible positive and negative environmental impacts deduced from basic characteristics of nanotechnologies

Basic characteristic, quality	Possible environmental effects or ecological impacts	
	Positive	Negative
Small size and mobility of particles	Targeted use for ecoefficient technology, for reduced resource consumption	Penetration of the lung and alveoli, penetration of cell membranes and blood-brain-barrier, Mobility, persistence and solubility as indications for bioaccumulation and environmental risk
Defined structure, particle size or layer thickness, purity	Targeted use for ecoefficient technology, for reduced resource consumption	Sophisticated production processes, higher material and energy flows, increased resource consumption
Material quality	Possible substitution and replacement of substances toxic for man and environment	Health and environmental risks due to problematic (rare) elements or substances, if used in open systems
Adhesion, cohesion, agglomeration	Inherent safety due to tendency of nanoparticles to adhesion, cohesion and agglomeration	Behaviour of nanoparticles or nanofibres in the environment; nanoparticles could mobilise toxins or heavy metals or mediate their uptake
Novel chemical effects, altered behaviour	Targeted use for ecoefficient technology, for reduced resource consumption	Altered solubility, reactivity, selectivity, catalytic effects, photocatalytic effects, unexpected technical, chemical, toxic and ecotoxic effects possible due to temperature-dependency of phase transitions
Novel physical effects, altered optical, electrical, magnetic properties	Targeted use for ecoefficient technology, for reduced resource consumption	Requires ultraclean and highly defined "technical environments". In case of technical failure, unexpected effects could occur due to novel physical effects
Self-organisation	Targeted use for ecoefficient technology, for reduced resource consumption	Within the vision of self-replicating nanorobots, risk of uncontrolled development, if precautionary measures for containment and control are not sufficient

Source: Steinfeldt et al. 2004, p. 2-3, modified

Several **environmental benefits** can be expected from the use of nanotechnologies for biomedical applications. In general, reduced resource consumption in terms of energy feedstocks and auxiliaries and reduced emissions could be realised in production. In the use phase, reduced resource consumptions could be due to small volumes and high specificities, e. g. in lab-on-a-chip applications in diagnostics and analytics (Türk et al. 2005a) or due to drugs with high specificities and effectiveness. Moreover, highly toxic substances (e. g. radioactive markers in certain diagnostic procedures) could be substituted by less toxic ones. In recent years, it has become an issue of both environmental chemistry and policy to minimise the discharge of pharmaceutically active compounds (PhACs) into the environment. The main route of emission is a diffuse release of the drug substance and/or its metabolites by patients into the environment with urine or faeces, followed by further dispersion and an eventual uptake by man and living organisms in the food chain<sup>30</sup>. This problem in the after-use or disposal phase could also be reduced if, due to nanotechnologies, fewer amounts of drugs could be used or excreted.

However, hardly anything is known to which extent and under which conditions the above-mentioned general environmental benefits could become effective in the biomedical field. For example, reducing the resource consumption of production processes is of subordinate importance for new and innovative drugs due to high performance and quality requirements of the both the process and the product, and due to pricing strategies. However, the aspect of reduced resource consumption may be relatively more important for drugs and devices with incremental improvements and with more intensive competition on a cost basis (e. g. generic drugs). In addition, it should be kept in mind that the sophisticated production processes for nanostructures could well lead to a much higher resource consumption in production processes than for conventional products, because they e. g. involve high temperatures or toxic chemicals. Whether the small volumes, related to more effective drugs or miniaturised analytical and diagnostic procedures, translate into reduced environmental burdens does not depend on the volumes only, but also the biological effects of the substances, their persistence and accumulation in the environment etc. Whether e. g. labs-on-a-chip also lead to waste re-

---

<sup>30</sup> According to Article 8 of the Directive 2001/83/EC on the Community code relating to medicinal products for human use an "indication of any potential risks presented by the medicinal product for the environment" is required in the application for obtaining an authorisation to place a medicinal product on the market. This applies in particular to new active substances, but not to orphan drugs. Draft guidance how to perform an environmental risk assessment of medicinal products for human use has been published by the European Medicines Evaluation Agency (EMA) for consultation in January 2005.

duction in the after-use phase, depends to a large extent on product concepts, e. g. single-use devices, or their recycling or reuse.

As a consequence, life cycle assessments and related tools should be used to identify potential environmental benefits and costs already in early stages of technology and product development in order to shape them accordingly. This has already been performed for several applications of nanotechnologies<sup>31</sup>, but – to the best of our knowledge – not yet for biomedical applications. In the field of cosmetics, sun cream with nanoparticles would be a useful example.

**Environmental risks arising from nanoparticles** will be dealt with in more detail in chapter 3.4.

Finally, the potential environmental impacts of **autonomously acting nanorobots** which might also be able to self-replicate, has been addressed as an issue of concern, albeit this is a rather far-in-the-future scenario ("grey goo<sup>32</sup>"). The deliberate or unintentional release of such nanorobots would most likely be irreversible and would pose the difficulty to track and control their dispersal in the environment. The option of an international ban of the development of such systems has been suggested in the context of military uses of nanotechnologies (see chapter 3.11).

### 3.4 Health and environmental risks associated with nanoparticles

In recent years, concerns have been expressed that products of nanotechnologies may pose a risk to human health and the environment due to the nanoparticle structures involved (see e. g. ETC Group 2003b; ETC Group 2003a; Paschen et al. 2003; Health and Consumer Protection Directorate General of the European Commission 2004; The Royal Society & The Royal Academy of Engineering 2004; Aitken et al. 2004; Luther, (ed) 2004; Swiss Re 2004; Tomellini, de Villepin 2005; Mark 2005; SCENIHR 2005; de Jong et al. 2005; Löchtfeld et al. 2005a; Balshaw et al. 2005). These concerns are based on the following considerations (SCENIHR 2005):

---

<sup>31</sup> E. g. nano-lacquers and -varnishes, process innovation in styrol synthesis, displays, light, suncream (Steinfeldt et al. 2004); automobile catalysts (Lloyd et al. 2005) and nanocomposite materials for use in automobiles (Lloyd, Lave 2003).

<sup>32</sup> Grey goo is a term first used by molecular nanotechnology pioneer Eric Drexler in his book "Engines of Creation". The term refers to a hypothetical end-of-the-world event involving molecular nanotechnology in which out-of-control self-replicating robots consume all life on Earth while building more of themselves. It is usually used in a science fictional context ([http://en.wikipedia.org/wiki/Grey\\_goo](http://en.wikipedia.org/wiki/Grey_goo)).

- *Health risks of particulate matter.* Health risks are well-known which are due to exposure of humans and animals to particulate matter, e. g. to ultrafine dust. Although it is unclear how this can be extrapolated to toxicity of nanoparticles, it gives an indication for possible effects.
- *Changes in properties due to size.* Nanotechnologies exploit characteristic changes of material properties and behaviour which are due to the small size of the materials. If changes in properties are exploited for beneficial effects, the biological effects of the materials could also be changed in a way that may be detrimental to health and the environment. It is already well established that toxicological and ecotoxicological data obtained for the bulk material are not reliable in predicting the toxicological and ecotoxicological properties of the same material in nanoparticulate form. Although there is no evidence yet, it cannot be ruled out that unique adverse effects could occur which have never been observed for chemicals in other physical forms.
- *Mobility across biological barriers.* The mobility of nanoparticles across biological barriers is exploited in drug delivery systems, but could also lead to unintended mobility of nanoparticles in the body after their uptake.
- *New, not naturally occurring substances.* In addition to the small size, new substances such as fullerenes and carbon nanotubes are exploited in nanotechnologies. They do not occur naturally and their biological effects are not yet well understood.

**Nanoparticle sources** are on the one hand natural phenomena, on the other hand they are unintentionally produced and released in several "classical, familiar" human processes such as cooking, material fabrication and transportation (internal combustion, jet engines). Relatively new is the production and intentional or unintentional release of engineered nanoscale components which occur either in the workplace or in consumer products (or, in the case of nanomedicine, in medicinal products or medical devices). Presently, it is not known how significant the increase in exposure due to intentionally engineered nanoparticles is, and will be in the future (SCENIHR 2005, p. 17).

Two types of nanostructures have to be distinguished with respect to exposure:

- Nanoparticles can be an integral feature of larger objects (e. g. in the form of nanocomposites and nanocrystalline solids) which are thought to pose a low risk as long as they remain fixed. In medical applications, such immobilized nanostructures can be found inside or on surfaces of medical devices such as surgical implants, but may be released due to continuous chemical processes and/or mechanical stress at the interface of implants and surrounding tissues (de Jong et al. 2005).
- Nanoparticles may also occur as free nanoparticles. In medical applications, this is the case e. g. in novel drug delivery systems. In free form, nanoparticles pose a higher risk.

**Nanoparticle emission**, intentionally or unintentionally, can occur during R&D, manufacturing, during use, and after use/during disposal, and after their dispersion in the environment. **Exposed groups** comprise

- *Patients*. Patients are intentionally exposed to nanoparticles during diagnosis or treatment, but may also be unintentionally exposed, e. g. if clearance of nanoparticles from the body after completed diagnosis or therapy takes longer periods of time, if implants release nanoparticles due to wear or chemical processes, or if nanoparticles move to non-target organs due to their mobility.
- *Staff*. Occupational exposure of staff involved in R&D, manufacturing, diagnosis and treatment, disposal, recycling, remediation and cleaning, transport and trade, and accidents must be taken into consideration. It has to be noted that typically, workers are exposed to higher levels of chemicals and for longer periods of time than the general population.
- *General population*. The general population may mainly be exposed to nanoparticles from medical applications due to re-exposure through the environment. Local populations in the vicinity of R&D, manufacturing or medical facilities such as hospitals or waste disposal sites may be exposed to nanoparticle emissions from these sites.

In principle, **uptake** of nanoparticles may occur via inhalation, dermal exposure or ingestion. For medical applications, injection and implantation are additional, very relevant and specific routes of uptake. While inhalation of nanoparticles is the uptake route that has, up to now, been investigated relatively extensively, hardly anything is known about the other routes of uptake, and the biological fate of the nanoparticles in the body (e. g. distribution, accumulation, metabolism, organ specific toxicity).

There is consensus that the present level and scope of knowledge is insufficient in order to carry out a risk assessment, comprising exposure assessment, hazard identification, hazard characterisation and risk characterisation. For risk assessment, sufficient knowledge would have to be available regarding

- *Nanoparticle characterisation*. Presently, there is a need to establish appropriate methodologies for nanoparticle characterisation and routine measurements. It is already established that the traditional mass concentration is not sufficient. It will also be required to measure the number of particles and/or their surface area. Moreover, there is a need for internationally harmonised nomenclature.
- *Exposure evaluation*. For exposure evaluation at workplaces and in the environment, equipment needs to be developed for routine measurement in various media. Moreover, methods need to be developed which allow the determination of the environmental fate of nanoparticles and their detection in the environment, and new sampling techniques and strategies for exposure assessment should be elaborated.
- *Physiological responses to nanoparticles*. The knowledge about the toxicology and ecotoxicology of nanoparticles must be broadened. In addition to nanoparticle char-

acterisation, hardly anything is known yet about dose-response relationships, the transport of nanoparticles in the human body, their distribution, accumulation, metabolism and persistence in the human body as well as in the environment. Moreover, the mechanisms of toxicity need to be elucidated at sub-cellular and molecular levels. One mechanism is the induction of reactive oxygen species, leading to oxidative stress. This bears the potential that nanoparticles could exacerbate pre-existing medical conditions. Based on such findings, conventional toxicity and ecotoxicity tests may require modification.

- *Epidemiological studies.* In order to better characterise possible health risks due to nanoparticles, monitoring of occupational exposure is important. Moreover, epidemiological data on the potential impact of nanoparticles on human health are required.

Impacts for regulatory approval of new chemicals, nanotechnologies-enabled medical devices, medicinal products and cosmetics are outlined in chapter 3.7.1.

### **3.5 Equal access and just allocation of resources**

#### **3.5.1 Introduction**

Fairness is one of the key principles of biomedical ethics which translates into the goal that there should be equal access to nanotechnologies-enabled medical diagnostics, therapies and services for all those in need of it. However, the concern is often brought forward that this equal access may be challenged in nanotechnologies, leading to a "nano-divide". This term has been coined in analogy to the "digital divide"<sup>33</sup> (Mnyusiwalla et al. 2003; Baird, Vogt 2004; Invernizzi, Foladori 2005) and implies that there will be both winners (i. e. countries, parts of the population, certain companies or other relevant players who have access to nanotechnologies and benefit from it) and losers (i. e. players with limited access to or capabilities to exploit the benefits of nanotechnologies, but may be affected by negative impacts and risks), and that this is in conflict with the ethical principle of fairness.

In the following paragraphs, we will outline what may be understood as "equal access" for various applications and levels of nanotechnologies in the biomedical sector, what

---

<sup>33</sup> The digital divide is a social/political issue referring to the socio-economic gap between communities that have access to computers and the Internet and those who do not. The term also refers to gaps that exist between groups regarding their ability to use information and communications technologies effectively, due to differing levels of literacy and technical skills, as well as the gap between those groups that have access to quality, useful digital content and those that do not. The term became popular among concerned parties, such as scholars, policy makers, and advocacy groups, in the late 1990s (<http://en.wikipedia.org>; accessed Oct 27, 2005).

is understood by "equal access", who the winners and losers might be, for which reasons, how deep the resulting or imminent nano-divide might be, and what can or should be done to avoid its formation or its deepening. There is a close link to the social and ethical issue of governance (see chapter 3.8), because those with a weak position in decision-making are likely to belong to the losers.

### **3.5.2 Macro-socioeconomic impacts of access to nanotechnologies for biomedical applications**

On an international and macro-economic level, access to scientific-technical know-how in nano(bio)technologies and access to applications, products and services derived from it are seen as a prerequisite to support on the one hand the goals of reaching or maintaining economic competitiveness in international competition. On the other hand, it could support an increase in quality of health care, which by itself could contribute to inner security and social peace (see also chapter 3.11) as well as to quality of life. By contrast, if access to know-how is impaired, also the attainment of these goals may be at stake. Among the instruments employed to reach these goals are research policy, patents, and (international) cooperation.

#### **3.5.2.1 Priorities in research policy**

With respect to **research policy**, nanotechnologies for biomedical applications would, in a first step, have to be defined as a research priority within nanotechnologies (see Wagner, Zweck 2005, chapter 4). Developing nanotechnologies for health applications is also among the research priorities that are fully supported and called for in participatory fora involving the general public (e. g. citizens' juries; see chapter 3.12). Moreover, fine-tuning within such a research priority would be required in order to actively strive for realising the benefits of nanomedicine while avoiding its risks, posing the question of how future trajectories of nanomedicine can be steered towards serving the public good. Here, decision support tools within the framework of Health Technology Assessment (HTA) could be more widely used, among them health economic assessments, cost-benefit-assessments, and evaluations, which systematically analyse properties, effects, and/or impacts of health care technology and procedures with respect to costs and/or health effects. Moreover, there are close connections to governance issues (see chapter 3.8). In addition, serving the public good could also comprise the allocation of sufficient resources to research into the health and environmental effects of nanoparticles, as outlined in chapter 3.4 and recommended by many (e. g. Paschen et al. 2003; The Royal Society & The Royal Academy of Engineering 2004; Health and Consumer Protection Directorate General of the European Commission 2004; Tomellini, de Villepin 2005; Mark 2005; SCENIHR 2005; de Jong et al. 2005). It also

raises the question which research resources should be allocated by developed countries to support research into applications which would be especially of benefit for developing countries. A "Global Dialogue on Nanotechnology and the Poor: Opportunities and Risks"<sup>34</sup> is presently ongoing in the USA, carried out by the Meridian Institute and sponsored by The Rockefeller Foundation (US) and International Development Research Centre (Canada) (see also chapter 3.12).

### 3.5.2.2 Patents

While patents can work as beneficial instruments for the protection of intellectual property, they also bear the potential to contribute to deepening the "nano-divide" both between countries as well as between companies or (global) corporations and countries. The latter could be the case especially if patent claims are very broad, e. g. by cross-industry patent claims which span several industry sectors, or by claims which relate to whole classes of nanoparticulate substances and materials (ETC Group 2005b). There is concern that such broad claims could stifle innovation (The Royal Society & The Royal Academy of Engineering 2004). Moreover, it bears the potential that patent monopolies could arise in certain fields. In this case, patent owners might get significant influence over certain trajectories of nanotechnologies development, and be in a gate-keeper position, thus determining access and price for licences, excluding non-patent holders and those not able or willing to pay licence fees. This could mean that poorer countries could be prevented from access to much needed medication, as has been the case (outside nanotechnology) e. g. in producing generics of drugs for AIDS treatments (Invernizzi, Foladori 2005). The influence of policy on these decisions may be limited if the patent holders are private corporations, without the obligation of democratic legitimation. So one of the main issues of concern here is ownership and control (see also chapter 3.8). To which extent the above-mentioned – and general, not specific for nanotechnologies – disadvantages of patents become true for nanotechnologies, depends to a large extent on how broad the patent claims can be, how strict the criteria of novelty and non-obviousness and distinction between discovery and invention are interpreted in practice (Stipkala 2005), e. g. whether a known (and patented) drug can also be patented in nanoparticulate form. This remains a challenge mainly for patent offices.

Moreover, the ethical challenge where to draw the borderline of patentability of nanotechnology inventions is still to solve, especially, if, as is most likely in biomedical

---

34 <http://www.nanoandthepoor.org/>

applications, living organisms or their components are involved. In addition to the above-mentioned governance and control issues, this raises the ethical questions of

- the patentability of living matter or of atoms as basic building blocks of nature,
- whether such patents would offend against public policy or morality and thus would qualify as non-patentable,
- whether human dignity is protected (GAEIB 1993; GAEIB 1996).

This has already been a major controversial issue in the biotechnology field (e. g. with the campaign "No patents on life"), and it could well be that the controversial discussion could also extend to nanotechnologies. An indication for this could be that the technology-critical civil-society group Action Group on Erosion, Technology and Concentration (etc-group) has already addressed the issue (ETC Group 2005b; see also chapter 3.12.4).

### **3.5.3 Resource allocation in health care systems**

One issue subsumed under the "nano-divide" term is the concern that not all patients who could benefit from nanotechnologies-enabled diagnostics, therapeutic interventions or services would have equal access to them. This concern relates on the one hand to the question whether health care systems in poor countries will be in the position to provide them. On the other hand, in developed countries, access to advanced diagnostic and therapeutic options often depends on whether such interventions are reimbursed by statutory or private health insurances, or whether the patient has to pay for it himself. Given the fact that most nanotechnologies-enabled products and services will not come at lower costs than their conventional counterparts with which they compete, only those patients able to afford the costly interventions would have access. On the other hand, if the limited (!) health care resources were generally spent on expensive nanotechnologies-enabled interventions when the same health effect could be achieved in a more cost-effective way with alternative interventions, this would also prevent other patients from access to appropriate treatments, because of the misallocation of scarce resources.

Against this background, there is a need for fairness and transparency in such resource allocation decisions. This means that the decisions should be oriented towards the health outcomes that are to be achieved in a cost-effective way. This could imply a comparative assessment of nanotechnologies-enabled interventions with alternative options to achieve the objective, in order to avoid that certain options are unduly favoured over others. Health technology assessments, health economic assessments and a systems perspective, taking the entire disease management process into ac-

count, would substantially support the knowledge base for and transparency of such decisions.

### **3.5.4 Prerequisites for taking advantage of extended options for self-determination**

As outlined in chapter 3.2, nanotechnologies-enabled diagnostic and therapeutic interventions will provide extended options for self-determination with respect to one's health, especially through predictive testing and risk specifications in early, asymptomatic stages of disease. However, in order to use these options for one's benefit, certain skills and abilities will be required (Rohr, Schade 2000). Among them are the willingness and motivation to care for one's future life, to have the means and motivation to alter one's way of living in order to avoid or reduce health risk factors in case a predisposition for a disease is detected, to cope with this knowledge of an imminent health threat, and to invest in disease prevention. In order to avoid a "nano-divide" in this respect, information and education of patients as well as enabling them to take self-responsibility for their health is important.

### **3.5.5 Right not to use available options**

The broadening of options to exert self-determination with respect to one's health also bear the downsides that it could, under perceived or factual social pressure, also turn into a duty for self-responsibility in a context where diseases are no longer perceived as "fate", but as "preventable", especially, if population screening schemes are introduced. In this context, patients could be exposed to factual or perceived discrimination, if they do not make use of the predictive testing and risk specification options available. This requires a broader debate about the question to which extent man can be held responsible for his own life and health, and how this responsibility can in practice be balanced with the right not to know and with patient's autonomy.

## 3.6 Privacy

### 3.6.1 Overview of relevant privacy issues and measures to guarantee privacy

The issue of privacy is especially relevant for nanotechnologies applications in medical diagnostics which is a near-term development in *in vivo* imaging and *in vitro* diagnostics (Wagner, Zweck 2005, chapters 8 and 9). With respect to social impacts and ethical deliberations, one can build on an extensive analysis in the genetic testing and pharmacogenomics/pharmacogenetics field (see e. g. CIOMS Working Group on Pharmacogenetics 2005; The Royal Society 2005; Kollek et al. 2004) as well as the telemedicine/ambient intelligence field (see e. g. Friedewald, Da Costa 2004; Friedewald et al. 2005). Despite these links to similar issues, a nano-specific analysis is nevertheless desirable for the following reasons:

- The nanotechnologies community is – at least in part – not fully aware of and familiar with the debate in the above-mentioned fields,
- Nanotechnologies-enabled diagnostics have specific features and imply both a new quality as well as new contexts of diagnostic procedures, which make certain social implications and ethical consideration even more important and/or mean a shift in emphasis. This is outlined in more detail in the excursus on nanodiagnostics and nanoanalytics in chapter 3.6.2.

The major concern regarding privacy is the potential misuse of the very sensitive and personal data obtained by the above-mentioned procedures. In related fields, the following safeguards against potential misuse have been discussed and – partly – implemented. They could also serve as a guidance for the debate of nanotechnologies-related issues:

- *Free and informed consent.* A consequence from the ethics principles of autonomy and self-determination is the mandatory requirement for free and informed consent, before a diagnostic procedure is performed. However, there are several critical points which must be resolved for a given diagnostic procedure and its context in order to reduce the risk that sensitive personal information is collected, stored, distributed, integrated and analysed without adequate consent:
  - *Scope of the consent.* It must be resolved to which scope and which use of data the consent relates, to which extent and in which form (e. g. anonymised form) will the data be made available to third parties.
  - *How informed?* Some future nanotechnologies-enabled diagnostic or analytic procedures may technically allow covert surveillance, without consent and knowledge of the person surveyed. Another important aspect is that it is well known

from genetic testing that, although extensive information and counselling of the person to be tested is required, the provision very often is of substandard quality and quantity (see e. g. Ibarreta et al. 2004; Hennen et al. 2000). This situation will most likely also occur for nanotechnologies-enabled diagnostics and analytics or will even worsen if a broader diffusion of these diagnostic procedures into (non-specialist) clinical practice takes place. In addition, several diagnostic procedures are likely to be performed on persons with impaired ability to understand the consequences of testing or not testing their conditions. This impaired ability may be due to (young) age, cognitive impairment, a low level of education, disease or disablement. For these especially vulnerable groups, specific efforts for counselling or protecting them from undue interventions are required.

- *How free?* As outlined in chapter 3.5.5, patients could see themselves exposed to perceived or factual social pressure and discrimination if they wish to make use of their right not to know and do not make use of the predictive testing and risk specification options available. This is especially likely if the notion prevails that diseases are no longer "fate", but are preventable.
- *Purpose of tests.* Nanotechnologies-enabled diagnostic and analytic procedures bear the potential to be used for a broad variety of purposes, including defined medical purposes, research involving human beings, criminal investigations as well as national security, surveillance and control, testing for workplace and for insurance purposes. Against this background, there is a clear need for political control and legitimisation for which purposes personal data, which allow the identification, classification and evaluation of individuals, may be collected and analysed in order to avoid discrimination, social control and to ensure civil rights.
- *Data access and use.* There is concern regarding an appropriate confinement of data access and use, especially if personal data are increasingly interlinked. There is concern that information may be concentrated in the hand of those with the resources to develop, run and control such networks.

Summarising, it can be stated that the challenge lies in operationalising the above-mentioned principles in practice and in the resolving of conflicting interests in a fair way. Moreover, it may be required to establish whether current regulatory frameworks and institutions provide appropriate safeguards to individual or group privacy (The Royal Society & The Royal Academy of Engineering 2004, p. 54).

### **3.6.2 Excursus: Nanodiagnostics and -analytics**

In addition to the issue of privacy (chapter 3.6), nanotechnologies applications in medical diagnostics have also significant other social impacts and ethical implications which will be outlined in this excursus. This excursus serves as an example how the analysis of social and ethical implications of nanotechnologies on the one hand can build on an extensive analysis in related fields (e. g. genetic testing, ambient intelligence), but on

the other hand implies a shift of emphasis to certain issues. Nanodiagnostics and –analytics have also been chosen because they are a development which is rather close to clinical application (Wagner, Zweck 2005; Türk et al. 2005a).

### 3.6.2.1 Specific features and characteristics of nanodiagnostics and nanoanalytics

It is expected that nanotechnologies-enabled diagnostics and analytics will enable a significant extension in various dimensions of present capabilities to diagnose and analyse. These features, in their sum, can only be achieved by a convergence of nanotechnologies with bio- and IC technologies:

- *Range of testable conditions.* It is expected that the range of testable conditions (e. g. body functions and states, diseases or disease predispositions) will significantly expand, and that tests at the cellular or molecular level will become available.
- *Time and frequency.* Testing will become possible at earlier disease states (i. e. before clinical symptoms become manifest) and even before an elevated individual risk is suspected (i. e. screening), resulting in an increase in predictive testing. It is likely that also the frequency of testing will increase, in order to monitor the progression of disease or the effects of therapeutic or preventive interventions, and even continuous surveillance and control can be expected.
- *Occasions for testing.* While biomedical diagnostics are presently performed mainly for diagnostic purposes if clinical symptoms or at least an elevated individual risk is suspected, new occasions are likely to emerge: general screening for preventive purposes, for specification of individual risk, for monitoring of health status if a higher individual risk has been identified, and continuous surveillance.
- *Sites of testing.* In addition to specialists, testing will also be performed by non-specialist doctors and laboratories, by the care staff or the patient himself; with an increase in point-of-care and home testing.
- *Populations tested.* Broader segments of the population will be subjected to testing, e. g. to healthy people without clinical symptoms, to children, newborns and unborns, to tissues and gametes.
- *Data acquired.* Both the quantity of data acquired will increase, but also the quality will change: In case of continuous surveillance of at-risk patients, data on behaviour, activity profiles and life style will inevitably also be acquired. Moreover, the risk of incidental findings, i. e. information about conditions where there was no intention to obtain them, will increase (see e. g. Illes et al. 2004; Illes et al. 2002). The sheer increase in quantity and quality of highly sensitive personal data and the increasing abilities to interlink and process them makes the need for privacy and data protection even more pressing.

- *Linking diagnostics to intervention.* Especially in surveillance applications, deviations from normal conditions will trigger interventional procedures.

### **3.6.2.2 Impacts for privacy**

Concerns regarding privacy have been analysed in detail in chapter 3.6.1.

### **3.6.2.3 Quality assurance of tests and related counselling**

Given the likely rapid expansion of testable conditions and test systems, there is a clear need for validation and quality assurance of the tests, especially if they will increasingly be applied outside specialists' facilities and increasingly provide predictive information. This does not only relate to genetic testing, but also to the testing of disease conditions in presymptomatic stages of the disease. However, already today, certification of testing facilities, quality assurance and counselling are not provided in the required quantity and quality (see e. g. Ibarreta et al. 2004; Hennen et al. 2000; Hüsing et al. 2005). Moreover, medical staff must be qualified to appropriately understand and interpret the results of the tests, which often only give a probability for a disease condition, in terms that are understandable by the patients and can be transformed into appropriate (changes of) behaviour.

Especially in surveillance applications and "intelligent" devices, the reliability of these complex systems and vulnerability to interferences is important. They may also pose new problems with respect to liability in case of failure (see also chapter 3.7).

### **3.6.2.4 Dealing and coping with information from diagnostic procedures**

Many concerns related to expanded options for diagnosis are not directed at the testing procedures themselves, but relate to the knowledge that is acquired in this way:

- *Gap between diagnostic and therapeutic capabilities.* While the diagnostic capabilities expand (as outlined in chapter 3.6.2.1), this is not necessarily the case for the abilities to treat and cure the respective disease or disorder, leading to a widening gap between diagnosability and curability. It also poses the question to which extent a diagnostic (predictive) test is justified if no appropriate therapeutic interventions can be offered to the patient.
- *Interpretation of test results.* Many diagnostic tests, especially if they are of predictive character, only give a specification of the individual risk in terms of increased probabilities. Whether the increased risk will, in the future, become manifest as clinical symptoms in the individual case, has inherent prognostic uncertainties. For both the medical staff as well as the patients it is very difficult to understand and interpret these test results, and to transform them into an appropriate behaviour. It could re-

sult in significant psychological stress for the patient and his relatives, if one feels the sword of Damocles hanging constantly above one's head. If a predisposition for a severe disorder or disease is diagnosed, this also bears the risk of (perceived or factual) discrimination, even if the disorder never becomes manifest in the individual case.

- *Incidental findings.* The more diagnostic tests are performed, the higher the probability of incidental findings, i. e. information about conditions where there was no intention to obtain them, and, because of the unintentional character, there are often no appropriate structures and provisions available or consistently enforced to deal with these findings, thus increasing the risk that privacy, patient autonomy and the right not to know, as well as access to counselling and psychosocial support, and other interests of the patient are at risk.
- *Medicalisation of deviations from normal status.* The more diagnostic tests are performed, the higher the likelihood that any deviations from a "normal" status are seen as pathologic and as requiring medical treatment. On the one hand, this poses the question what – in the light of the wide variability in living organisms – constitutes a "normal" condition and by whom and on what empirical basis this has been established, bearing also in mind that the definition of "normal status" has a clear cultural component (see also chapter 3.9). On the other hand, this could imply a "systematic hypochondria" and also a loss of confidence into one's own body, delegating the sensitivity to body signals to external surveillance systems and also delegating the responsibility for one's body and health to external monitoring and control. And finally, the tendency to medicalisation could also imply that other interventions than medical ones to the deviation could be neglected, although they may be equally effective.
- *Right not to know.* The more diagnostic tests are performed, the more the notion could prevail that people have a duty to perform (predictive) diagnostic tests, resulting in social pressure or discrimination if such tests are refused. Against this background, a broader debate is required about the question to which extent man can be held responsible for his own life and health, and how this responsibility can in practice be balanced with the right not to know and with patient's autonomy (see also chapter 3.5.5).

These issues underline the importance that extensive human testing must be embedded in appropriate structures in terms of quality assurance, counselling and psychosocial support, as has been outlined in chapter 3.6.2.3.

## 3.7 Regulation, control, liability

At present, no specific regulations exist in Europe which refer specifically to the production and use of nanoparticles either for workers', consumers' or patients' safety or for environmental protection, so that current rules and operational practices are applied.

In the view of the concerned public, the implementation and enforcement of appropriate and effective regulations and control are major instruments in order to limit possible misuse and potential risks (see chapter 3.12). In the shaping of appropriate regulations, governance issues (chapter 3.8) play an important role.

### 3.7.1 Regulatory impacts of possible risks of nanoparticles

At present, possible health and environmental risks are a major issue of debate (chapters 3.4), with possibly significant implications for regulation, once the still existing knowledge gaps have been narrowed through research in order to enable an appropriate assessment of the possible risks emanating from nanoparticles (SCENIHR 2005). In the directives which regulate market access for medicinal products and medical devices<sup>35</sup>, a risk assessment and management is already required in order to obtain market approval. However, researchers, manufacturers, notified bodies and competent authorities should be made aware of the need to carry out a dedicated (nano)toxicological risk assessment (de Jong et al. 2005). This risk assessment should especially take into account

- the biological fate of nanoparticles (distribution, accumulation, metabolism, organ specific toxicity),
- medical-specific uptake routes (injection, implantation),
- possible side effects, based on mechanisms of interaction of nanoparticles with living matter (e. g. formation of reactive oxygen species, exacerbation of preexisting medical conditions), and on transport in the body (e. g. ability to cross the blood-brain-barrier).

Appropriate and nano-specific test systems and assessment schemes for the above-mentioned may still have to be developed (SCENIHR 2005), so that the development of specific guidance documents at a European level for the safety evaluation of

---

<sup>35</sup> For medical devices, the regulatory requirements are laid down in the three European Directives 93/42/EEC (Medical Devices Directive), 90/385/EEC (Active Implantable Medical Devices Directive) the (MDD), 93/42/EEC; and 98/79/EC (In Vitro Diagnostic Directive), for medicinal products, the directives 2001/83/EC (Medicinal Products for Human Use) and 2001/20/EC (Clinical Trials on Medicinal Products for Human Use) apply.

nanotechnology products applied in medical technology is strongly recommended (de Jong et al. 2005). Moreover, there will be a need for appropriate labelling and safety sheets.

In addition to the development of assessment schemes for medical devices and medicinal products which take the specificities of nanoparticles into account, it will also be required to investigate whether the present classification of products into medicinal products, medical devices or cosmetics is deemed appropriate to deal with the related nanoparticle risks. This is important because the regulatory requirements one has to comply with differ, depending on the relevant regulatory framework. The challenge is to strike the appropriate balance between ensuring high safety and quality standards for the patient, consumer and the public and making innovations and market access possible.

The issue of proper classification is also relevant with respect to the expectation that there will be an increase in "borderline products" which will be difficult to classify unambiguously, so that a "clearing house mechanism" in regulatory authorities might be required. Examples for such products are cosmetics with health claims, bio-hybrid artificial organs, and also autonomous intelligent medical systems. For the latter, it should be examined whether existing risk assessment and quality control schemes are sufficient to assess complex systems, operating with distributed decisions, and for which not all relevant conditions can be tested beforehand.

With respect to occupational health, new workplace standards will be required, as those established for dust are insufficient. Moreover, the establishing of occupational exposure limits for chemicals in the form of nanoparticles should be considered (SCENIHR 2005). Because it is insufficient to rely on knowledge of the classical toxicity testing of chemicals and materials when the risks of nanoparticles and nanostructures have to be assessed, it should also be considered whether nanoparticulate materials should fall within REACH (SCENIHR 2005; The Royal Society & The Royal Academy of Engineering 2004).

Moreover, an internationally harmonised terminology and nomenclature is required, as well as international cooperation in research and regulation. Nanotechnology expertise in regulatory authorities is of major importance to deal with these challenges and strike an appropriate balance between ensuring health, safety and quality and at the same time make innovation and commercialisation of nanotechnologies-derived products possible. Stakeholders' positions regarding the regulatory impacts of possible risks of nanoparticles are depicted in chapter 3.12.4.2.

### 3.7.2 Liability and insurability

It is in the interest of the public, of industry and policy that risks from nanotechnologies are insurable. At present, there are no special policy exclusions or terms in regular use that are tailored to address risks from nanotechnologies (Munich Re Group 2002; Swiss Re 2004; Hett, Herold 2005; Allianz, OECD 2005). In principle, the following types of damages and losses, to be covered by insurances, are possible:

- Personal injury, leading to workers' or patients' compensation,
- property damage, e. g. through dust explosion during manufacturing,
- financial losses, e. g. due to general and products liability, products recall,
- environmental damage, leading to environmental liability,
- third party liability.

Because it will not be possible at present and for a longer period of time, to quantify the probability of potential losses occurring and their possible extent, the insurance industry works with loss scenarios. These scenarios have the following basic characteristics (Allianz, OECD 2005, p. 43):

- occupational exposure is a major concern, with increasing numbers of persons being exposed to nanoparticles,
- causal relationships between action and damage will be difficult to establish in individual cases,
- dangers will be chronic rather than acute, harmful effects will evolve over longer time,
- increasing and high numbers of insurance holders (companies) are likely to be affected.
- thus, resemblance with major product liability cases from the past (e. g. asbestos).

Insurance companies fear ruinous loss accumulation from late claims, but presently do not seem to take a general exclusion of nanotechnologies from insurance cover into considerations. Rather, they aim at employing risk management and loss-limiting measures, such as excluding certain high-risk industrial activities from cover, active steering of the insurance company's portfolio, or detailed individual risk assessments (Allianz, OECD 2005). Their strategy also depends on the future development of the European regulation with respect to the burden of proof to establish liability.

### **3.7.3 Free will, responsibility and possible impacts for criminal law and justice**

There is concern that nanotechnologies-enabled ICT brain implants could significantly modify human behaviour and decision-making, posing the question whether it is the person or the device that "decides". If intelligent systems intervene substantially with control of human behaviour, to which extent can either man or the technical artefact be held responsible for his deeds? This poses on the one hand questions of liability for the device manufacturer. On the other hand, it could also challenge our ways of thinking about responsibility and blame, with possible, yet disputed impacts on the criminal law and justice, because our intuitions about a person's responsibility for his actions depends on a free will (Raeymaekers et al. 2004; Hüsing et al. 2005, chapter 21). This controversial discussion is presently being led in the neuroscience field, but could well extend also to nanotechnologies.

### **3.7.4 Military uses**

As outlined in more detail in chapter 3.11, Paschen et al. 2003, p. 366ff recommend to start deliberations whether existing preventive arms control frameworks for biological, chemical and nuclear weapons are sufficient or whether they should be amended to also cover nanotechnologies-derived weapons. In addition, nanotechnologies-related arms control measures should be initiated, such as e. g. trust-building measures and international cooperation, and – if their development is technically deemed feasible – an international ban of self-replicating nanosystems.

## **3.8 Governance**

Major concerns of the public with nanotechnologies, but also with new technologies in general, relate to governance and trust questions which cut across most categories discussed in this chapter 3. It is acknowledged that nanotechnologies bear the potential to be both beneficial as well as harmful, but that the outcome depends on the choices that are made in the further development of nanotechnologies (Arnall 2003). In this context, the critical questions are (The Royal Society & The Royal Academy of Engineering 2004)

- how future trajectories of nanotechnologies can be steered towards wider social goals and be exploited for the public good, whether the technology will be shaped in such a way that its outcomes will genuinely benefit society, the environment and people,
- to which extent alternative trajectories are also taken into account in order to reach these goals, and

- to which extent the rights and interests of all concerned stakeholders are respected, taken into account and balanced in a fair way in order to avoid a "nano-divide".

There is a prevailing lack of trust in the institutions usually in charge of dealing with these questions, e. g. policy and administration, multinational corporations, scientists etc and also in the instruments employed (e. g. research priorities, patents, liability). These concerns are mostly based on empirical lay knowledge about the past behaviour of institutions responsible for the development and regulation of technological innovations and risks which is considered to be unsatisfactory in many ways and as a consequence leads to a lack of trustworthiness of these institutions (Marris et al. 2001).

Marris et al. 2001 have also suggested key elements of consistent behaviour over a longer period, and across different fields, how to restore trust in these institutions, among them

- admitting uncertainty, and explaining how this has been taken into account in decision-making,
- utilising input from all relevant sources (not only scientific experts) in order to improve the knowledge base on which decisions are taken,
- being transparent about how decisions are made, including explanations how different interests, risks and benefits have been balanced against one another,
- imposing heavy sanctions in cases where mismanagement or fraud is identified,
- demonstrating that the views of the public are understood, valued, respected and taken into account by decision-makers – even if they cannot all be satisfied (Marris et al. 2001, p. 11).

Against this background, The Royal Society & The Royal Academy of Engineering 2004 (p. 64ff) have advocated for a broader stakeholders' and the public's involvement already in "upstream issues" by

- informing and educating people,
- learning about the public's and stakeholders' attitudes and preferences,
- incorporating public values in decisions,
- improving decision quality,
- resolving conflicts, and
- improving trust in institutions.

## 3.9 Enhancement

### 3.9.1 Introduction

Biomedical applications of nanotechnologies can not only be used to treat and restore impaired body functions, but also for enhancing them. Enhancement is understood as interventions which aim at an improvement of human abilities and performance beyond "normal" levels - also in an excessive and undesired manner (Friele, Fulford 2004).

Enhancement is not at all new or specific to nanotechnologies. Examples can be found in e. g. use of growth hormones in paediatrics, plastic and cosmetic surgery, doping in sports, or genetic engineering (Fuchs et al. 2002), and it is also discussed in neuroscience for cognitive, motor and sensory enhancement (Kennedy 2004; McGuire, McGee 1999; Wolpe 2002; Farah et al. 2004; Chatterjee 2004; Hüsing et al. 2005). Nevertheless, nanotechnologies, especially in their convergence with biotechnology and ICT, are often seen as powerful potential enablers to perform such interventions into a broad variety of motor, sensory and cognitive functions with unprecedented precision. As a consequence, enhancement of human capabilities has played a significant role in nanotechnologies visions (see e. g. National Science Foundation 2002), is envisioned for military applications (see chapter 3.11, e. g. soldiers with enhanced vision through retinal implants) and also conjures long-term visions of technologically enhanced man-machine hybrids ("cyborgs") (see also chapter 3.10). Human enhancement is prominently advocated by the transhumanists and extropiers. This is a sociocultural group which advocates "the moral right for those who so wish to use technology to extend their mental and physical (including reproductive) capacities and to improve their control over their own lives. [They] seek personal growth beyond [their] current biological limitations" and aim at "redesigning the human condition, including such parameters as the inevitability of aging, limitations on human and artificial intellects, unchosen psychology, suffering, and our confinement to the planet earth"<sup>36</sup>.

Apart from these utopian and far-reaching visions, a latent societal demand for enhancement of certain human functions (e. g. cognitive performance, alertness, mood, endurance) is not unlikely. Against this background, ethical deliberations and social debates are required whether there is a difference between helping someone whose capacities are below average to reach the average, and helping someone already above average to reach a still higher level of functioning (Friele, Fulford 2004).

---

<sup>36</sup> quoted from "The Transhumanists Declaration", see <http://transhumanism.org/index.php/WTA/declaration/>; accessed Oct 23, 2005

The present discussion whether enhancement can be seen as an ethically legitimate goal – inside or outside the medical profession – focuses on the arguments of fairness and justice, medicalisation of an increasingly wide range of aspects of human life, accomplishment, authenticity, and the moral status of human contingency (Fuchs et al. 2002), and an overview will be given in the following paragraphs<sup>37</sup>.

### **3.9.2 Blurred borderline between enhancement and treatment**

To choose health and disease conditions as a distinction whether interventions into human abilities and functions should be considered ethically legitimate or not is problematic because there is no fixed and clear definition of what can be considered as "healthy" or "normal". As a consequence, the borderline between "health/enhancement/illegitimate" and "disease/treatment/legitimate" is blurred. This is due to several factors:

- Broad biological variation of human functions, abilities and performance,
- Social, cultural and subjective elements play an important role in the perception of what is "normal", and are also subject to change,
- It is inherent to the interventional procedure that it can be both used for treatment as well as enhancement. One cannot have the treatment options without having the risk of using it also with the aim of enhancement.

### **3.9.3 Consistency of enhancement with ethos of the medical profession?**

In the debate, it is often brought forward that it is the physician's role to have (only) the duty to heal. In this context, this medical ethos is often seen as a certain precaution against the use of interventional methods for enhancement and against misuse and manipulations. This, however, would require a clear and operational distinction between treatment and enhancement which is difficult to draw. On the other hand, it can be argued that patient autonomy is increasing, and physician's duties also aim at improving patients' quality of life, so that physicians' roles could well also encompass enhancement if it contributes to the (subjective) improvement of an individual's quality of life. This could, however, lead to a "medicalisation" of conditions which could otherwise be considered as "beyond the normal limits" but now become a condition requiring treatment. It could also promote medical interventions as the preferred means of tack-

---

<sup>37</sup> The following text is a modified version of chapter 17 "Enhancement of cognitive functions" in Hüsing et al. 2005.

ling the underlying problem although interventional alternatives, which might be even more effective, may also be adequate.

### **3.9.4 Health economics perspective**

Interventions with an enhancement purpose also raise the health economic questions whether and under which conditions health care systems should provide and pay such interventions. On the one hand, the provision of such interventions could be rejected if a health care system is understood as a system which only has the duty to compensate impaired equality of opportunity if it is due to disease, and to restore it to a level which is the normal function within the species or relevant reference group of the population. It would be an unjust allocation of scarce resources to provide interventions beyond this level. On the other hand, it is argued that impaired equality of opportunity may already arise if the subject's abilities are still within the reference group range. If the perceived level of suffering were equivalent to suffering from disease, it could be considered unfair not to provide the intervention.

### **3.9.5 Principle considerations regarding the ethical legitimacy of enhancement**

In the context of enhancement through nanotechnologies, it is not sufficient to take a health care perspective, as has been done in the previous paragraphs. It is likely that nanotechnological enhancement would not be confined to the health care systems, and would also be carried out by other than medical professions.

A central general concern is equality and fairness. It is likely that access to enhancing interventions will not be equal, so that certain segments of the population will be favoured over others, thus leading to a further widening of socio-economic divide ("nano-divide"). This does not rule out the possibility that enhancement could be used by individuals to compensate for existing inequalities, and to narrow the socioeconomic gap. In this case, it has to be asked whether enhancement on the level of the individual should be the preferred means, or whether other means (e. g. changing social conditions) are ethically more acceptable in order to diminish socioeconomic disparities. In this context, the issue of accomplice arises: it is a controversial issue to which extent the interests of the affected individual should be followed by provision of enhancement – even if this perpetuates unfair and discriminating tendencies, or whether the individual's wishes should be denied due to these reasons. In this context, it is also argued that some forms of enhancement are not only chosen in order to achieve a competitive advantage, but for the sake of non-competitive, intrinsic benefits. If enhancement were

rejected in order to avoid socio-economic inequalities, the achievement of intrinsic benefits would also be ruled out.

The issue of medicalisation of problem-solving by biomedical enhancement has already been discussed above.

Biomedical enhancement also challenges the authenticity of an accomplishment. In e. g. contests or exams, not the achieved result or level of performance is important, but also whether it can be attributed to a person as his/her personal accomplishment. If the result is, however, achieved with the help of enhancement, this undermines the accomplishment. The risk that enhancement of human, especially cognitive functions may also alter the authenticity of a personality, a person's identity and autonomy, has already been discussed above.

And finally, enhancement has been understood by some authors as a means to override the human contingency, in the sense of fragility, imperfection and finitude, because humans are subject to chance and change. They reject enhancement due to the high moral status of these integral elements of the *conditio humana*, whereas groups as the transhumanists deny a high moral status of the *conditio humana*, and explicitly want to overcome its limitations.

### **3.10 Blurring the borderline between humans and technical artefacts**

A tendency within nanotechnologies for biomedical applications is the blurring of the borderline between humans and technical artefacts. There is a certain overlap with the issue of enhancement (see chapter 3.9), but also poses specific questions.

The use of technical artefacts or interventions for restoring or substituting impaired functions of the human body is an integral part of human culture, as exemplified by glasses for impaired vision, limb prostheses, dental implants, pacemakers and organ transplants. Against this background, the use of nanotechnologies in biomedical applications pose the question whether such applications bring about a new quality in the foreseeable time which might push the – culturally defined – borderline between humans and technical artefacts further (chapter 3.10.1), and if so, whether this borderline has a moral status and should therefore be fix to a certain extent, or whether it may or should be subject to change? The latter poses the question how far-reaching these changes and interventions may go.

### 3.10.1 Relevant technical trends

Among the technical trends with the potential to blur the borderline between humans and technical artefacts are

- Devices as replacements for or complementation of biological components, e. g. retinal or cochlear implants, artificial organs,
- Intimate integration of miniaturised devices into the human body (e. g. sensors, pacemakers, artificial organs),
- Interlinkage of humans with internal or external devices (e. g. remote surveillance and control, brain-computer interfaces), also hybrid systems of distributed action, i. e. interaction of humans with intelligent technical artefacts,
- "Humanisation" of devices (e. g. "intelligent" devices, autonomously acting systems, futuristic visions of self-replicating and autonomous nanorobots),
- Far-reaching visions, advocated e. g. by transhumanists (see chapter 3.9), which explicitly aim at deliberately crossing the borderline between humans and machines in order to overcome "human limitations".

### 3.10.2 Quality of intervention

One important question to be discussed in this context is whether it makes a difference to use e. g. glasses to restore impaired vision, or a pacemaker to support cardiac performance, or to realise devices depicted in chapter 3.10.1. Among the criteria for assessing these questions are

- availability of alternative options for restoring the impaired function,
- severity of the impairment,
- type of impaired function (vital/non-vital, cognitive or sensory/motor/metabolic function),
- extent (depth) of intervention, including external device or implant/transplant, (ir)reversibility of device use, controllability of the device by the patient vs. autonomously acting devices.

A new quality which may challenge human dignity, fundamental rights, integrity of the human body and non-instrumentalisation is especially seen in nanotechnologies-enabled interventions if (EGE 2005, p. 26)

- the devices cannot be removed easily (implants),
- they influence, determine or change cognitive and psychic functions, thus influencing human identity as a species as well as individual subjectivity and autonomy,
- they could be misused, due to their network capability, for all kinds of social surveillance and manipulation,

- they serve military applications (see also chapter 3.11),
- no clear distinction between therapeutic intervention and enhancement can be drawn (see chapter 3.9),
- if technology by-passes normal sensory experience,
- if implants influence future generations, biologically and/or culturally.

### 3.10.3 Concerns and possible impacts

In addition to concerns related to privacy (see chapter 3.6), informed consent (see chapter 3.5), difficulties to draw the borderline to enhancement (see chapter 3.9), fair access (chapter 3.5), which are covered elsewhere in this report, we will address here two fundamental concerns (Baumgartner 2004):

- *Possible impacts on our understanding of what makes humans human (conditio humana)*. What makes humans human is a central question in philosophy and religion. It also comprises the question against what humans can be distinguished in order to define their identity. In the past, these reflections related to borderlines between man and animal, or man and God. The developments depicted in chapter 3.10.1 could lead to the requirement to also reflect about the borderline between man and machine/technical artefacts.

In addition, basic to personal identity is the intimate relationship between bodily and psychic functions. This personal identity may be challenged if a major proportion of bodily or psychic functions is performed or supported by technical artefacts.

Autonomy is also considered a central characteristic of personal identity which would be, in hybrid systems of distributed action, be (partly) delegated to "intelligent" technical artefacts which act autonomously and adaptively, perhaps leading to emergent behaviour of the systems with properties that no individual component of the system has. On the one hand, this poses the more technical question how such systems can operate safely, effectively and in a coordinate and cooperative manner, how controllable they are and how unintended impacts of technical autonomy can be prevented (see also chapter 3.3). It also poses questions regarding liability, if these systems function in an unintended way (see chapter 3.7). And finally, our concept of a human being as well as human societies are based on the notion that human beings have a free will, a view that is currently being challenged by some in the view of recent findings from brain imaging studies (see e. g. Roth 2001; Wegner 2002; Singer 2003), and is very controversially being discussed (see e. g. Pauen 2004; Präsident der Berlin-Brandenburgischen Akademie der Wissenschaften 2004; Raeymaekers et al. 2004). If technical devices would interfere with the free will, then our ways of thinking about responsibility and blame would be challenged, with possible, yet disputed impacts on the criminal law and justice, because our intuitions about a person's responsibility for his actions depends on a free will (Hüsing et al. 2005, chapter 21). This discussion from the neuroscience/philosophy-field could also extend to nanotechnologies.

- *Moral status of "made" artefacts.* The question is also raised whether "made" artefacts which fulfil important criteria of known forms of living organisms can claim the moral and normative status that is currently assigned to humans, animals or other life forms.

### 3.11 Military uses

Biomedical applications of nanotechnologies bear the potential to be used both for civil as well as military purposes. At least in the USA, the Department of Defence is a major funding agency for nanotechnologies, carries out own research, and also several visions, goals and applications are clearly military. Among them are (Paschen et al. 2003, p. 127ff.)

- the use of nanotechnology drug delivery systems for the improvement of chemical and biological weapons,
- nanoparticles as or nanomanufacturing for the design of new classes of weapons,
- improved detection of biological and chemical weapons through nanosensors,
- enhancement of soldiers' performance in battles, e. g. by improved vision through devices such as retinal implants, or antimicrobial battle-suits,
- improved surveillance of the population or the enemy in espionage through nanosensors,
- manipulating widely-used nanosensors and delivery systems in order to harm the enemy forces and population,
- autonomous, perhaps self-replicating nanorobots with human-destructive potential ("Grey goo").

Moreover, a widening "nano-divide" (see chapter 3.5) could contribute to the aggravation of conflicts both within one country ("social peace" under threat) and between countries or regions.

Against this background, a US citizens' jury on nanotechnologies has recommended "that nanotechnology not be used to develop weaponry" (Kleinman, Powell 2005). There are concerns that nanotechnologies could trigger new forms of arms race, and that new forms of weapons could be developed which are not covered by existing arms control frameworks. Moreover, as civil and military R&D in nanotechnologies cannot be unambiguously be distinguished, it may be difficult to detect, monitor and control nanotechnologies weapons development programmes. As secrecy is an inherent feature of military R&D, this secrecy could fuel also the public's distrust in nanotechnologies R&D which may not be restricted to military R&D, but might also extend to clearly civil developments. As a consequence, Paschen et al. 2003, p. 366ff) recommend

- to increase transparency and provide information in order to make clear which nanotechnology developments and applications are civil, military or dual-purpose,
- to start deliberations whether existing preventive arms control frameworks for biological, chemical and nuclear weapons are sufficient or whether they should be amended to also cover nanotechnologies-derived weapons, and
- to initiate nanotechnologies-related arms control measures, such as e. g. trust-building measures and international cooperation, and – if their development is technically deemed feasible – an international ban of self-replicating nanosystems.

### **3.12 Public perception of and attitudes towards nanotechnology and nanobiotechnology in the medical sector**

#### **3.12.1 Media coverage of nanotechnology**

Mass media play a significant role in the shaping of public attitudes to nanotechnology because they are a major source of information for the general public. Moreover, they have a role as agenda-setters for public discourse and as gatekeeper who confer status on issues, stakeholders, and policy makers. Therefore it is of interest to examine

- to which extent nanotechnology has become an issue that is covered in mass print media (salience<sup>38</sup>),
- which themes are covered and how they are framed; i. e. what type of arguments are being mobilized, and
- what the proportion of stories with positive and negative assessments is.

Such studies have extensively been carried out for biotechnology. Meanwhile, several studies have also been carried out which address the media coverage of nanotechnology. They mainly focus on the USA and UK print media coverage of nanotechnology, and most of them are modelled on similar studies of biotechnology which allows – to a certain extent – a comparison of the media coverage of the two technologies. Table 3.2 gives an overview of published or ongoing studies on media coverage of nanotechnology.

---

<sup>38</sup> Salience is an indicator of the attention given to an issue.

Table 3.2: Overview of published studies on media coverage of nanotechnology

Country	Media analysed	Time period	Remarks	Source
UK	10 UK-based daily newspapers <sup>39</sup> and 8 UK-based national Sunday newspapers <sup>40</sup>	4/2003-6/2004	Framing of nanotechnology during period of rising public salience	Anderson et al. 2005
USA UK	New York Times Independent (London)	1990-2003	Analysis of risk and benefit coverage	Gaskell et al. 2004; Gaskell et al. 2005
USA UK	Selected US and UK newspapers and wire services	2000-2004	Conference abstract, no data published yet	Friedman and Egolf, 2005
USA	New York Times, Washington Post, Wall Street Journal, Associated Press	1986-2004	Comparison with media coverage of biotechnology, analysis of salience and framing	Gorss, Lewenstein 2005
USA	US newspapers, magazines, general interest publications (not specified) retrieved from ABI/Proquest database	1986-1999		Faber 2005
(mostly) USA	94 mostly US newspapers and popular periodicals national television and radio broadcasts	1988-2003	up to now quantitative analysis, content analysis in progress	Stephens, McKissick 2004
(mostly) USA	94 mostly US newspapers and popular periodicals	1988-mid2004	content analysis of 350 articles	Stephens 2005
(mostly) USA	(Mainly) US media available online and covered by the news portal Topix.net	12/2003-6/2004	Content analysis, topics: business, politics, SciTech, ELS concerns	Schummer 2004
not specified, reach of www.amazon.com	Nanotechnology books, available through www.amazon.com	2004	Purchase of nano-books from online-bookstore as indicator for public interest in nanotechnology; network analysis of co-purchase book data combined with content analysis	Schummer 2005

<sup>39</sup> The Times, The Guardian, The Daily Telegraph, The Independent, The Financial Times, The Daily Mail, The Daily Express, The Daily Mirror, The Sun, The Daily Star.

<sup>40</sup> The Sunday Times, The Observer, The Sunday Telegraph, The Independent on Sunday, The Mail on Sunday, The Sunday Express, The Sunday Mirror, The News of the World

The most extensive study has been conducted by Gorss, Lewenstein 2005 for the USA, whereas data from Europe are only available for the UK (Gaskell et al. 2005, and, most recently, from Anderson et al. 2005). In the following, we summarise the key results from these two studies. Because no studies have been published up to now which specify media coverage of biomedical nanotechnology applications, the results relate to media coverage of nanotechnology in general.

In the Gorss, Lewenstein 2005 study, a content analysis of all nano-related articles was carried out which had been published between 1986 and 2004 in three US elite newspapers (New York Times, Washington Post, Wall Street Journal) and one general newspaper (Associated Press). The content analysis comprised the classification of the themes<sup>41</sup> covered in the articles, as well as the frames<sup>42</sup> (the context in which the themes are presented). The main findings can be summarised as follows:

- Nanotechnology coverage in the selected US newspapers remained on a low level of only a few articles per year from 1986 to 1998. From 1999 onwards, media coverage increased strongly and steadily over time, reaching more than 150 articles in 2003, and is expected to rise further in the coming years.
- Media interest in nanotechnology began to spread from the opinion-leading elite press which mainly addresses leaders in America also to a wider public addressed by the general press in 2003, which corresponds to a time delay of approximately 4 to 5 years.
- Media coverage of nanotechnology throughout the entire period is overwhelmingly positive. This is due to two factors: on the one hand, articles about applications and finance dominate the coverage, and these tend to be inherently more positive in tone. On the other hand, articles about nanotechnology risks are clearly negative in tone, but are less prevalent. In addition, the positive stories tend to be much more positive than the negative stories are negative.

---

41 Six themes were distinguished: 1. proposed and actual uses of nanotechnology ("Applications"), 2. current legislation ("policy"), 3. bipartisan support or disagreement, federal monies issues ("politics"), 4. investment reports, economic opportunities ("financial"), 5. "safety and risks", and 6. "Others".

42 Nine typologies of framing for nanotechnology were applied: 1. report of technical development, nanotechnology represents the "wave of the future" ("Progress"); 2. nanotechnology's effect on the economy ("Economic Prospects"); 3. Nanotechnology is either morally necessary or morally repugnant ("Ethical"); 4. Developing nanotechnology will create unforeseen ills ("Pandora's box"); 5. Nanotechnology may spiral out of human control ("Runaway"); 6. Coverage about ethical, legal, and societal implications; influence over research and development ("Public Accountability"); 7. Applications from nanotechnology will be in the distant future ("Long Way Away"); 8. Nanotechnology represents a confluence of technologies including biotechnology, information technology, and cognitive science ("Confluence"); 9. "Others".

- With respect to the framing, the vast majority of articles tend to frame nanotechnology in terms of progress and economic prospects. From these data it can be concluded that the analysed media mainly present nanotechnology as a distinctive new source of progress.
- The "public accountability frame"<sup>42</sup> arises early and remains present throughout. It appears about as often as the "scary science fiction scenarios" which are represented by the frames "Pandora's box" and "Runaway" and address nanotechnology as uncontrollable. According to the authors, this may be due to the media reflecting that the public is worried more by questions of trust and credibility than by risks and "scary science fiction scenarios".
- Nanotechnology media coverage appears to be event-driven rather than issue-driven.

### **Comparison of nanotechnology media coverage USA - UK**

While these data relate to newspaper coverage in the USA, Gaskell et al. 2005 performed a comparative analysis of nanotechnology coverage in the US newspaper New York Times and the UK newspaper Independent. This study confirms the results of Gorss, Lewenstein 2005 that the media interest in nanotechnology does not begin before 1999, and that there is subsequently a steady and strong rise of nanotechnology coverage in the press. This holds true for both the USA and the UK. However, the rather low number of articles is seen as an indicator that nanotechnology is only just appearing on the radar screen of press and public attention. Moreover, in both countries benefits of nanotechnology (e. g. advances, improvements of any kind) are more often reported than risks (e. g. threats, dangers). However, there was considerably more reference to benefits in the New York Times than in the Independent, rendering UK media coverage of nanotechnology less overwhelmingly positive than in the USA. Three sources dominated the increasing risk coverage in 2002/2003: the publication of Michael Crichton's novel "Prey" (2002), the publication of the ETC group reports (ETC Group 2003b; ETC Group 2003a) and, especially, a speech of Prince Charles in 2003 (Anderson et al. 2005). Further monitoring of the media coverage is required to decide whether US media keep on reporting much more positively about nanotechnology than UK media.

### **Comparison of nanotechnology and biotechnology media coverage in the USA**

The media analysis of Gorss, Lewenstein 2005 also allows a comparison of US media coverage of nanotechnology with biotechnology in its early stages. The key findings are:

- In both technologies, the media coverage shows a similar pattern regarding the time course and amount of articles. Media interest in biotechnology started in 1977-1980, whereas media attention for nanotechnology became apparent from 1999 onwards.
- Both technologies in their early stages are predominantly framed as "progress".
- Therefore, the media coverage of both biotechnology in its early stages as well as of nanotechnology seem to follow a similar pattern in terms of salience and framing which might point to a common pattern of "emerging technologies".
- The framing as "progress" was much more dominant in biotechnology in its early stages, where overall strongly positive assessments and hardly any "negative" frames were reported in the articles. By contrast, nanotechnology is presented in the media not as overwhelmingly positive as was biotechnology; negative frames and especially the "public accountability" frame are included much earlier and at a more significant level. The reasons for this difference have not yet been analysed. Among the hypotheses discussed are
  - having learnt the lessons from the very controversial and polarised biotechnology public debate in biotechnology, trying to "avoid the same mistakes with nanotechnology",
  - inherent feature of nanotechnology as an issue,
  - effect of the current public climate where people seem to be more inclined to pay attention to risks and possible impacts (of technologies).
- Most articles for biotechnology as well as nanotechnology can be appropriately classified according to the chosen themes and frames. However, two frames associated with biotechnology ("Nature/nurture"-frame, "Globalization"-frame) are not (yet?) pertinent to nanotechnology. On the other hand, nanotechnology media coverage employs two new frames<sup>42</sup>, "Long way away" and "Confluence" which are not prominent for biotechnology.

### 3.12.2 Public opinion – knowledge and attitudes as revealed in surveys

Since 2002, several surveys have been completed which aimed at elucidating the (general) public's knowledge of and attitudes towards nanotechnology. An overview of these surveys is given in Table 3.3.

Table 3.3: Overview of surveys of the general public's knowledge of and attitudes to nanotechnology

Country	Population sample analysed	Time of survey	Remarks	Source
EU 15	15,000; 1,000 in each EU member state	Sept-Oct 2002	Part of the Eurobarometer 55.2 survey, random probability survey, face-to-face interviews	Gaskell et al. 2004; Gaskell et al. 2005
USA	850	Dec 2002 to Feb 2003	Random probability survey, telephone interviews	
EU25	32,897 citizens, aged 15 or above; appr. 1,000 or 500 in each country EU25 Member States, Candidate countries (Bulgaria, Romania, Croatia, Turkey) and EFTA countries (Iceland, Norway, Switzerland)	Jan-Feb 2005	Part of the Eurobarometer 224 and 225 survey, random probability survey, face-to-face interviews	Eurobarometer 224 and 225, wave 63.1, special survey "Europeans, Science and Technology" <sup>43</sup>
UK	1,005, aged 15 or over	Jan 8-14, 2004	Representative quantitative three-question survey, part of a larger face-to-face survey Two workshops for qualitative results	The Royal Society & The Royal Academy of Engineering 2004; BMRB 2004
DE	1,019 general population, aged 14 and above	Sep 10-19, 2004	Random-digit dialled survey, face-to-face interviews	komm.passion GmbH 2004

<sup>43</sup> [http://europa.eu.int/comm/public\\_opinion/archives/ebs/ebs\\_224\\_report\\_en.pdf](http://europa.eu.int/comm/public_opinion/archives/ebs/ebs_224_report_en.pdf);  
[http://europa.eu.int/comm/public\\_opinion/archives/ebs/ebs\\_225\\_report\\_en.pdf](http://europa.eu.int/comm/public_opinion/archives/ebs/ebs_225_report_en.pdf)

Table 3.3 continued

Country	Population sample analysed	Time of survey	Remarks	Source
USA	3,909	Oct 2001	Non-random internet survey, 3 nano-items within the larger Survey2001	Bainbridge 2002
USA	1,536 general population, aged 18 years or older	Late March to early April 2004	National random probability telephone survey	Cobb, Macoubrie 2004
USA	1,536 general population, aged 18 years or older	Late March to early April 2004	Experiment embedded in the telephone survey; participants were presented different framings of nanotechnologies	Cobb 2005
USA, Texas	978 students and staff of University of Texas Pan America, > 18 years of age, not related to science and engineering fields	not specified; 2004 likely	Multiple choice questionnaire	Sheetz et al. 2005
USA	706	Fall 2004	Representative, carefully constructed probability sample, national telephone survey	Scheufele, Lewenstein 2005; Lee et al. 2005

The more extensive and detailed surveys have addressed the following questions:

- What does the public currently know about nanotechnology?
- Which attitudes prevail in the public?
- How does knowledge about nanotechnology affect attitudes towards it?
- Which role do risks play? Do they dominate public perceptions, or is there a balanced view of risks and benefits?
- What is the role of social embedding of nanotechnology?

Although the surveys are difficult to compare in detail because of important differences in how the questions were asked and how the answers were recorded, there are several common findings:

- *Low awareness.* In general, the awareness of the general population of nanotechnology in all countries surveyed is low. For example, only 29 % of all respondents in

the UK survey had heard of nanotechnology (The Royal Society & The Royal Academy of Engineering 2004, p. 59; BMRB 2004); in Germany, a share of 45 % was found (komm.passion GmbH 2004); and according to a US survey 48.2 % of the respondents had heard of nanotechnology (Cobb, Macoubrie 2004). In the 2005 Eurobarometer survey, nanotechnologies received by far the lowest rate of interest among the suggested eight items, with a mere 8 % developing interest in this field<sup>43</sup>. This, however, represented a doubling of interest compared to the 2001 survey where only 4 % of the respondents showed interest in nanotechnologies.

- *Little factual knowledge.* In accordance with the low awareness of nanotechnology, the factual knowledge is even lower in the general population. For example, only 19 % of all respondents in the UK survey could offer some definition of nanotechnology (The Royal Society & The Royal Academy of Engineering 2004, p. 59; BMRB 2004); in Germany, 15 % could specify what they associate with nanotechnology (komm.passion GmbH 2004); and in the USA, respondents on average could answer correctly only one of three factual true or false questions about nanotechnology (Cobb, Macoubrie 2004).
- *Overall positive assessment, more benefits than risks.* First exploratory surveys into the public's attitudes towards nanotechnology found a very positive assessment of nanotechnology. In a US internet survey of a segment of the population which is more likely to be positive about science and technology, 57.5 % of the respondents supported the statement that "human beings will benefit greatly from nanotechnology", whereas only 9 % agreed with the statement that "our most powerful 21<sup>st</sup> century technologies - robotics, genetic engineering, and nanotechnology – are threatening to make humans an endangered species" (Bainbridge 2002). In a US survey of the general population, the majority of Americans expected improvements (50 %) from nanotechnology regarding our way of living, 35 % of US respondents didn't know, whereas "no effect" was assumed by 12 % and "will make things worse" by only 4 %. Similar patterns prevailed in the EU15 regarding the "no effect" and "will make things worse" answers, but significantly less Europeans expected improvements (29 % of EU respondents) while the majority (53 %) answered "don't know". These results can be interpreted that people in the USA are more likely to take an optimistic stance on the (yet) unknown technology whereas the majority of Europeans adopts a wait-and-see position (Gaskell et al. 2004; Gaskell et al. 2005).

In 2005, the following attitudes towards nanotechnologies were found in the EU25: "Positive effects" on our way of life in the next 20 years were expected by 48 % of respondents, "no effect" by 4 % and "negative effects" by 8 %, and 40 % didn't know. Compared to the results obtained two years earlier, the share of undecided respondents had decreased significantly, as had the share of those assuming positive effects of nanotechnologies<sup>43</sup>.

- *Benefits and risks.* Some surveys address the questions which benefits and risks the public expects or fears from nanotechnology. In the USA, respondents could choose only one risk and one benefit from a list of five potential benefits or risks as the most important one to obtain or avoid. "New ways to detect and treat human

diseases" clearly scored highest among the benefits (chosen by 57 % of respondents), followed by "New ways to clean the environment" (16 %), "Increased national security and defence" (12 %), "Physical and mental improvements for humans" (12 %) and "Cheaper, better consumer products" (4 %). Regarding the risks, there was no similarly clear consensus which risk was perceived to be the most important one to avoid. "Losing personal privacy" scored highest (31 %), followed by "arms race" (24 %), "breathing nanoparticles that accumulate in the body" (19 %), "economic disruption" (14 %) and "uncontrollable spread of nanorobots" (12 %). Which benefits or risks were chosen was largely independent of the respondents' level of knowledge of nanotechnology (Cobb, Macoubrie 2004).

The survey in Germany also covered expectations and fears related to nanotechnology. As in the USA, use of nanotechnology for medical progress and environmental protection, as well as for economic growth was supported by more than 60 % of the respondents and rated as very positive (average score 2.5-2.8 on a scale of 1 to 6 (1 = strong support, 6 = strong rejection)). On the other hand, only 38 % "are afraid of nanoparticles which cannot be seen, heard or felt", whereas 50 % reject being afraid of them (komm.passion GmbH 2004).

Scheufele, Lewenstein 2005 found no significant influence of the awareness of nanotechnology on the perceptions of risks, but of benefits: respondents aware of nanotechnology perceived the benefits stronger than the unaware respondents, whereas no significant difference between the two groups was found regarding the risks.

- *Emotions.* Because emotions also play an important role in the construction of attitudes, Cobb, Macoubrie 2004 in their US survey also explored emotional reactions to nanotechnology. Most Americans hold positive, not negative emotions when asked how they feel about nanotechnology, with the absence of negative emotions being even stronger than the presence of positive emotions (70 % hopeful, 84 % not worried, and 95 % not angry).
- *Trust and social embedding of nanotechnology.* In the USA, the majority of respondents report low trust in business leaders within the nanotechnology industry to minimize risks to humans (60 % answer "not much", 40 % "somewhat" or "a lot") (Cobb, Macoubrie 2004). In Germany, 50 % of the respondents support the statement "The risk of companies using nanotechnology in an irresponsible way is too large". The survey in Germany reveals preferences regarding the social embedding of the future development of nanotechnology (komm.passion GmbH 2004):
  - Support of independent basic research which also addresses dangers and risks (supported by 69 % of respondents, score 2.1),
  - Stronger governmental control of nanotechnology (supported by 64 %, score 2.6),
  - Clear labelling of products produced with the help of nanotechnology (supported by 60 %, score 2.7),

- Research of nanoparticle effects on the environment prior to placing nanoparticle-containing products on the market (supported by 53 %, score 3.0).

All in all, the combined findings from the surveys show that levels of awareness of nanotechnology as an issue and levels of perceived knowledge are very low. Nevertheless, (even) in the absence of relevant scientific or policy-related information, people form opinions and make judgements about nanotechnology. Their opinions are currently influenced by factors other than factual and nanotechnology-specific information. Among these influencing factors are attitudes towards science and technology in general, scientific literacy, emotions, and cognitive shortcuts (e. g. personal predispositions, such as religion, ideology) and heuristics which are often provided by the mass media (for media coverage of nanotechnology, see chapter 3.12.1). Popular metaphors such as the "grey goo" have not been taken up widely and significantly by the general public, as benefits and positive emotions prevail. This perception, however, depends strongly on the social and regulatory context in which nanotechnology is embedded (Cobb, Macoubrie 2004; Scheufele, Lewenstein 2005; Priest 2005).

### **3.12.3 Focus groups and Citizens' juries**

Because surveys of the general public's attitude towards nanotechnology revealed a prevalence of "uninformed opinions about nanotechnology", findings from these surveys are of very limited value for the identification of genuinely considered beliefs about nanotechnology. In order to address this issue, some qualitative methods such as focus groups and workshops have been applied. Moreover, "upstream engagement" of citizens by participatory elements such as citizens' juries or consensus conferences have been started. As can be seen from the overview in Table 3.4 and

Table 3.5, most activities so far have taken place in the USA and the UK. Additional dialogues will be performed in EU countries within recently started EU-funded projects, such as Nanologue<sup>44</sup>, Nanobio-RAISE, and NanoDialogue (Monk, Rachamim 2005).

---

44 <http://www.nanologue.net>

Table 3.4: Selected focus groups on nanotechnology

Country	Instrument	Date	Remarks	Source
UK	Two moderated workshops with participants from the general public London (23 participants) Birmingham (27 participants)	not specified; late 2003 likely	Commissioned by the Royal Society and the Royal Academy of Engineering; Workshops aimed at exploring the participants' ideas about and attitudes towards nanotechnologies, the everyday concepts that people might use to understand and interpret the technology, and to identify and discuss areas for concern and questions they might have.	BMRB 2004; The Royal Society & The Royal Academy of Engineering 2004, p. 59ff
USA	Experimental issue groups in three different cities	2004	Participants were provided with background materials on nanotechnology and possible scenarios. Data were collected from the participants regarding attitudes, levels of concern for risk, trust in government and industry, individual level reflections and insights, demographic data.  Funded by the National Science Foundation	Macoubrie 2005; Macoubrie 2006
USA	12 groups with a total of 177 participants in 3 locations, representative of the demographics in the respective locations Spokane, Washington Dallas, Texas Cleveland, Ohio	May-June 2005	Participants were provided with balanced, clearly-written information on nanotechnology and on US regulatory and policy making bodies relevant to nanotechnology.  Part of the Project on Emerging Nanotechnologies at the Woodrow Wilson International Center for Scholars, in partnership with the Pew Charitable Trust	Macoubrie 2005

Table 3.4 continued

Country	Instrument	Date	Remarks	Source
USA	<p>Global Dialogue on Nanotechnology and the Poor: Opportunities and Risks:</p> <p>Paper on nanotechnology implications for the poor</p> <p>online-consultation (300 people registered, 600 comments received)</p> <p>Multi-Stakeholder Dialogue Meetings</p>	2005	<p>Carried out by the Meridian Institute, sponsored by The Rockefeller Foundation (US) and International Development Research Centre (Canada)</p> <p>The dialogue goals are</p> <ul style="list-style-type: none"> <li>• Raise awareness about the implications of nanotechnology for the poor;</li> <li>• Close the gaps within and between sectors of society to develop an action plan that addresses opportunities and risks, and</li> <li>• Identify ways that science and technology can play an appropriate role in the development process.</li> </ul>	<a href="http://www.nanoandthepoor.org/">http://www.nanoandthepoor.org/</a>
Austria	196; Students at the University of Innsbruck, staff at the Competence Centre for Alpine Risk Management, Innsbruck	March 2005	<p>Non-random sample</p> <p>3X2 factorial analysis on risk perception of nanotechnology</p>	Wiedemann, Schütz 2005

Table 3.5: Citizens' juries on nanotechnology

Country	Instrument	Date	Remarks	Source
UK	Citizens' jury 20 UK citizens	April- Sep 200 5	<p>The Citizens' Jury aims to:</p> <ul style="list-style-type: none"> <li>to provide a potential vehicle for people's informed views on nanotechnology to have an impact on policy</li> <li>to facilitate a mutually educative dialogue between people with diverse perspectives and interests</li> <li>to explore the potential for deliberative processes to broaden discussions about nanotechnology research policy</li> </ul> <p>Sponsored by the IRC in Nanotechnology at the University of Cambridge, Greenpeace UK, the Guardian and the Policy, Ethics and Life Sciences Research Centre at the University of Newcastle.</p>	<a href="http://www.nanojury.org">www.nanojury.org</a>
USA	Madison Area Citizen Consensus Conference on Nanotechnology 13 citizens from the Madison area	April 2005	<p>Organised by University of Wisconsin-Madison, Rural Sociology</p> <p>Sponsored by the Nanoscale Science and Engineering Center at the University of Wisconsin and the UW Integrated Liberal Studies Program</p>	Kleinman, Powell 2005 <a href="http://www.lafollette.wisc.edu/research/Nano/">http://www.lafollette.wisc.edu/research/Nano/</a>
Australia	Citizens' Panel on Nanotechnology Public engagement workshop with self-selected participants, some of them associated with civil society groups; Melbourne, Australia	April 2005	Organised by CSIRO as a component of the SEI Nanotechnology Scoping Project	Katz et al. 2005

From moderated workshop discussions as performed in the UK (BMRB 2004; The Royal Society & The Royal Academy of Engineering 2004, p. 59ff) and the USA (Macoubrie 2005; Macoubrie 2006), the following key findings can be derived:

- *Major benefits anticipated.* Workshop participants anticipate major benefits from nanotechnologies. In addition to acknowledgement of the general high potential of nanotechnologies for a broad range of applications and its contribution to general progress, possible contributions to medical applications, i. e. the development of new diagnostics and therapeutics are especially emphasised. In addition, benefits are expected with respect to new materials, environment, energy, consumer products, and improved food and nutrition, and positive impacts on employment and international competitiveness are anticipated.
- *Uncertainty.* A major theme in the workshops is the uncertainty associated with nanotechnologies. This relates to the anticipated benefits as well as the risks and the possible future balance of benefits and risks, the possible trajectories along which nanotechnologies might develop in the future, the untried nature of nanotechnology, and possible unforeseeable and long-term effects.
- *Many aspects of concern.* In the workshops, many aspects of concern were brought forward. Among them were the uncertainty and unknown effects of nanotechnologies, health risks, long-term and side effects, use of nanotechnologies in a way that was not perceived beneficial for society (e. g. military applications, impaired social freedom and stronger control), negative impacts for the developing world, insufficient control of nanotechnology, uneasiness with the governance of decision-making in nanotechnologies, and "playing God/messing with nature"; see also Table 3.6.
- *Low trust in government, suspicions of industry.* Many concerns related to role and behaviour of governmental as well as corporate institutions in decision-making about nanotechnologies. Trust is low that these players will recognise and manage risks of nanotechnologies proactively and appropriately, and will set priorities in a way that nanotechnologies develop along trajectories that are socially beneficial and do not only serve the interests of few (e. g. corporations, stakeholders, countries). Rather, it is suspected that e. g. corporations could gain too much influence and put economic interests before safety and general social benefits.
- *High demand for effective regulation and control.* In order to control anticipated health and environmental risks as well as to avoid that economic interests win over safety aspects, there is a high demand for the application of the precautionary principle, more testing of nanoproducts before their placing on the market, and the proactive research into long-term and side effects. Moreover, the enforcement of effective regulation, not only compliance with voluntary standards is called for – but at the same time people are sceptical whether governmental bodies will do the job properly because trust in them is low.
- *Governance issues, public engagement in technology decision-making.* In accordance with low trust in players such as governmental bodies and corporations which

presently play a dominant role in nanotechnology decision-making, there is a strong desire for public engagement in nanotechnology decision-making. On the one hand, workshop participants wish more transparency and to be more informed about the role and behaviour of the institutions which are involved in decision-making. On the other hand, they wish "public voices" to be directly involved in decision-making in order to ensure that in technology development, socially beneficial trajectories are being followed.

Table 3.6: Concerns related to nanotechnology, as identified in workshops with 177 US citizens

Concern	Percentage
True unknowns	13
Regulatory concerns	13
Human health risks	13
Testing and research for safety	12
Effect on the environment	10
Food and food chain concerns	7
Industry irresponsibility	7
Privacy	6
Military uses, international political instability	6
Playing God, messing with nature	4.5
Economic access and education	4
Consumer knowledge and information	3
People-centred goals for progress	1
Taxpayer cost of development	1
Fearful people stopping good	1
Mistrust of government in general	1
Social upheaval and adjustment	0.5
Total (N=426)	100

Source: Macoubrie 2005, p. 11-12

In addition to such workshops, citizens' juries are an instrument for public engagement in decision-making which on the one hand allow citizens a say in decisions about science and technology issues which may affect their lives, and on the other hand may offer insights or give emphasis to issues that experts would not consider in this way.

Up to now, one citizens' jury on nanotechnology was held in the EU (

Table 3.5). NanoJury UK was held in Halifax, Yorkshire, UK during the spring and summer 2005. It was sponsored by the IRC in Nanotechnology University of Cambridge, Greenpeace UK, the Guardian and the Policy, Ethics and Life Sciences Research Centre of the University of Newcastle. After being presented with information and perspectives from a range of different witnesses, the citizens' jury discussed the evidence amongst them and made up 20 recommendations, of which 10 recommendations received majority support from jury members whereas the other recommendations were supported only by a minority. The recommendations are presented in Table 3.7. Because formal and informal links have been established between the UK Nanojury and nanotechnology-related policy makers, the Nanojury recommendations are likely to receive political attention and have a certain policy impact.

Table 3.7: Recommendations made by the UK citizens' jury on nanotechnology in autumn 2005

Recommendations, supported by majority of nanojury members	Recommendations, supported by only a minority of nanojury members, with others unsure or against it
<b>Call for public involvement</b>	
A committee of public and representatives of a range of social groups and faiths should decide when, at key stages in technology development, public juries should be set up to look at public research spending. Public juries should also have a role in private research money to look at the ethical and social/environmental impacts. More consultation and information in plain English.	Normal citizens should decide when nanotech starts getting used in ICTs.
<b>Research/application priorities</b>	
If public money is spent, it should go on solving longer-term issues such as health and environmental problems. There should be incentives and strings attached for the private sector. Government should set up partnerships with nations leading in technologies that can improve health. New safe and effective nanomedicines should be available without discrimination. Government grants for development, manufacture and use of solar energy technologies. Support for nanotechnologies that bring jobs to UK.	Nanotechnologies should only be allowed if they develop wealth for everyone.  More wind turbines should be put at sea for the production of greener energy in case nanotechnology will not provide sustainable energy Nanotechnologies should be used to run electricity cables more efficiently and underground
Nanotechnologies will only be good if they lead to more quality leisure time.	

Table 3.7 continued

Recommendations, supported by the majority of nanojury members	Recommendations, supported by only a minority of nanojury members, with others unsure or against it
<b>Regulation and control</b>	
Manufactured nanoparticles should be tested as if they were a new substance, labelled in clear English, and tested in controlled environments before release.	There should be less ethical controls and government red tape, in order to avoid strangulation of inventiveness and loss of international competitiveness.
	Misleading adverts should be prevented by the advertising standards authorities for nanotechnology products where there is uncertainty about health and safety.
	Radiation and other health hazards associated with ICT should be kept low enough so that children can use phones and other ICTs safely; this could be achieved with the help of nanotechnology.
<b>Information and transparency</b>	
More openness on spending of public research money on nanotechnology.	
Scientists should improve their communication skills and encourage schoolchildren into a career in science.	
<b>Prevention of adverse impacts</b>	
	Poor people should be able to decide the prices of new technologies (e. g. new ICT) that are put on the market
	Certain ICTs (e. g. search engines, maps, language translators, educational sites) should be made free to people in serious debt and in poverty, so that they are given the opportunity to learn about new subjects and reduce inequalities.
	ICT companies everywhere should ration the amount people are able to use their ICT (automatic shut-off after over-use of communication time), in order to avoid that poor people become poorer.

Source: <http://www.greenpeace.org.uk/MultimediaFiles/Live/FullReport/7249.pdf>; accessed Oct 19, 2005; own editing

### 3.12.4 Non-governmental organisations (NGOs) – Involvement and positions

#### 3.12.4.1 Overview

At the present stage of development of the public debate about nanotechnologies, only few non-governmental organisations (NGOs) have developed a position, communicated it and taken a prominent and visible role in the debate in the EU. The majority of potentially affected non-governmental organisations<sup>45</sup> in the field of biomedical applications of nanotechnologies are still in an earlier stage of engagement: while the importance and relevance of nanotechnologies and their possible impacts have been acknowledged by many NGOs, the prevailing activity is the monitoring of the development. The monitoring comprises the designation of persons within the organisation who are responsible for this monitoring, and closely following relevant publications and activities such as conferences, workshops etc. Depending on the further course of nanotechnology development and the public debate as well as on organisation-internal strategies and resources, a more active engagement or even projects or campaigns are not ruled out for the future, but are not yet in a concrete conception phase. This assessment of the present stage of the public debate and the involvement of NGOs was unanimously given by all experts interviewed for this study.

In accordance with the focus of the present activities on research policy and the identification and first exploitation of economic potentials of nanotechnologies, **science and industry organisations** have advocated for public RTD funding in the field of nanotechnology, and emphasised the potentials of nanotechnologies and their importance for international competitiveness and have also been involved in related policy processes. Noteworthy is the early and prominent engagement of insurance companies, documented by several studies and position papers (Munich Re Group 2002; Swiss Re 2004; Allianz, OECD 2005) which has not been observed in other key technologies.

According to the experts interviewed, only two **civil-society groups** have gained international visibility and influence in the field of nanotechnologies: the Canadian based Action Group on Erosion, Technology and Concentration (etc group) and Greenpeace

---

<sup>45</sup> This relates mainly to consumer organisations, environmental organisations, civil society groups, and industry unions. We are not aware of patient organisations which have genuinely engaged in nanotechnology issues.

UK. The ETC group<sup>46</sup>, formerly RAFI - the Rural Advancement Foundation International – is an international civil society organisation which analyses technological information, provides information and analysis of socioeconomic and technological trends and alternatives to civil society organizations and develops strategic options related to the socioeconomic ramifications of new technologies. According to its own mission statement, it supports socially responsible developments of technologies useful to the poor and marginalized, addresses international governance issues, and monitors the ownership and control of technologies and the consolidation of corporate power. The head of ETC, Pat Mooney, is known for this fight against Monsanto's genetically modified seeds. In early 2003, the ETC group called for (ETC Group 2003b; p. 72):

- an immediate moratorium on commercial production of new nanomaterials,
- the launch of a transparent global process for evaluating the socio-economic, health and environmental implications of the technology,
- proposed the development of an International Convention for the Evaluation of New Technologies in order to make informed decisions about risks, benefits and ultimate value of emerging technologies, and
- called for the participation of citizens in open, informed debates.

The group also published reports on

- possible health and environmental risks of nanoparticles (ETC Group 2003a),
- the impact of nanotechnologies on food and agriculture (ETC Group 2004),
- political developments in policy and public debate (ETC Group 2005a) and
- patent issues of nanotechnologies (ETC Group 2005b).

In contrast to the ETC Group, Greenpeace takes a much more balanced position. Key person is Greenpeace UK's chief scientist, Doug Parr. In the report (Arnall 2003) and subsequent papers (Arnall, Parr 2005; Parr 2005), the potential of nanotechnologies to be used for both good and bad purposes is acknowledged and a differentiated opinion, depending on the applications and taken the present uncertainties into account, is advocated. Against this background, the process and the knowledge base, on which decisions about future trajectories of technology development are taken, are emphasised. There is a call for broadening the knowledge base especially regarding effects of nanoparticles, for transparency and information, and for upstream stakeholder and citizens' involvement in political decisions. As a consequence, Greenpeace UK has been one of the major initiators and supporters of the UK citizens' jury on nanotechnology (see chapter 3.12.3). A moratorium is not supported by Greenpeace.

---

<sup>46</sup> <http://www.etcgroup.org/about.asp>

According to the experts interviewed, other NGOs, if monitoring nanotechnologies at all, have not yet formed or published an "official" opinion, but may be in the process of doing so. The above-mentioned publications and positions by the etc group and Greenpeace are used as a major input in this process.

#### **3.12.4.2 Debate about health and environmental impacts of nanoparticles**

In the last years, a debate about possible health and environmental risks of engineered nanoparticles has developed. It is mainly an expert debate in which the relevant professionals (scientists from toxicology and ecotoxicology, industry representatives, representatives of relevant governmental bodies and agencies responsible for scientific advice of government, for surveillance and control of public and occupational health and the environment, insurance companies) are involved, both on national as well as international (EU, OECD) levels. Consumer and environmental groups monitor the debate, but have not yet taken an active part in it.

According to the experts interviewed, there is consensus among the different players in both national as well as the international (EU) debate with respect to the following aspects:

- The acknowledgement of both potentials and risks of nanotechnology,
- the need for an early, open and constructive dialogue,
- need for action regarding
  - standardisation, common nomenclature, availability of reference materials,
  - further research into potential risks of nanoparticles and expositions along all stages of the life cycle of products,
  - further development of test systems,

whereas different views prevail regarding the question whether and which need for regulation results. Moreover, only few stakeholders know and reflect the interests of the other stakeholders involved. The following positions can broadly be distinguished:

- *Industry.* The main interest is the development and commercial exploitation of new products and services through nanotechnology. Product and process safety in relation to liability claims play an important role for investments in R&D. Existing regulatory regimes are deemed sufficient. Transparency is supported as long as protection of economically important know-how is guaranteed.
- *Governmental agencies, administration.* Governmental agencies are in the process of defining their responsibilities and tasks with respect to nanoparticles and start developing strategies. They aim at supporting the further development of nanotechnologies.

- *Environmental, consumer and civil society groups.* Environmental, consumer and civil society groups aim at preventing or reducing risks for the environment, consumers and workers. They want to critically monitor the developments. They support increased research into the identification and assessment of risks. Environmental and consumer groups aim at increasing the transparency for consumers and citizens and therefore support measures such as product labelling.
- *Science and research.* Science and research see themselves as service providers in order to close knowledge gaps. Moreover, they hope for more research funding.
- *Unions, occupational health.* Unions as well as public and private professionals dealing with occupational health want to examine whether the existing precautionary and protective measures and regulations need amendment and adaptation.

These positions have also been described for stakeholders in Germany by Löchtefeld et al. 2005b.

### 3.13 Conclusions

In this report, an overview of the social and ethical issues of nanotechnologies is given, based on the analysis of recent reports, studies and other grey literature, scientific literature, discussions at conferences and workshops, and interviews with stakeholders, academics and administration staff with an excellent knowledge of the field. This overview comprises the following lines of analysis:

- An overview of social and ethical issues of nanotechnologies which are especially relevant for policymakers and decision-makers (chapters 3.2-3.8<sup>47</sup>),
- Ethical and philosophical deliberations of possible impacts of nanotechnologies with respect to enhancement and blurring the borderline between technical artefacts and living organisms, especially humans (chapters 3.9-3.10),
- Stakeholder attitudes towards and public perception of nanotechnologies (chapter 3.12).

All in all, the analysis shows that it has been widely recognised that there is a need to address social and ethical issues of nanotechnologies in addition to scientific, economic and political issues (as analysed by Wagner, Zweck 2005). Moreover, the ethical and sociological reflection should rather not be considered as an "add-on" which follows scientific-technological research and development, but should accompany it as an integral part. It is hoped that a better understanding of the interaction and mutual interdependence of science, technology and society could lead to more informed decisions about how to shape the development of nanotechnologies, and that mistakes that have

---

<sup>47</sup> Military uses (chapter 3.11) were included for reasons of completeness

been made with other technologies, such as biotechnology and genetic engineering, might be avoided by dealing proactively with the social and ethical embedding of nanotechnologies.

However, the systematic exploration of social and ethical issues of nanotechnologies has begun only recently. Due to the early stage of nanotechnologies, these are mainly basic and general deliberations about possible social and ethical issues for nanotechnologies in general. The majority of these analyses relates to nanotechnologies in their entirety, but is not (yet) differentiated to certain application areas or subfields of nanotechnologies (e. g. to nanomedicine) or to specific product lines (e. g. drug delivery). Moreover, because the development of nanotechnologies applications is a rather long-term endeavour, the exploration of social and ethical issues is hampered by the inherent uncertainty of this process and by the uncertainty about the future social contexts into which the use of the respective applications should be embedded. As a consequence, this report gives an overview of all issues discussed in the context of nanotechnologies, and makes specific reference to nanomedicine, where possible and appropriate.

It is striking that the current discussion of social and ethical issues of nanomedicine applications focuses on applications which are significantly different from the actual nanomedicine research and development which is pursued by public and private research institutions and companies: Whereas drug delivery systems play by far the largest role in current research and commercialisation efforts in nanomedicine (see Wagner, Zweck 2005), they have not at all been specifically analysed with respect to their social and ethical issues. One focus of social and ethical deliberations is on nanomedicine applications which are still in an embryonic stage, especially nanotechnologies-enhanced diagnostic procedures (e. g. in vitro diagnostics and imaging agents, see chapter 3.6.2). In this area, crucial issues from the social and ethical perspective are: purposes of diagnostic tests, dealing with the information thus obtained, quality assurance and qualification, informed consent, privacy and non-discrimination. Although a debate about similar issues is already well-developed in the field of genetic testing, there is nevertheless also a need to debate these issues in the context of nanotechnologies for various reasons:

- different (scientific) and stakeholder communities are involved which may not be fully aware of the debate in analogous fields,
- nanotechnologies-enabled diagnostics may have specific features which are different from genetic testing, and may be performed in other institutions and structures so that measures developed for genetic testing may not be fully appropriate for nanotechnologies-enabled diagnostic procedures and may need adaptation.

Social and ethical analyses of nanotechnologies also deal to a substantial extent with the potentially disruptive character of nanotechnologies which has generally been claimed for nanotechnologies, among them also futuristic visions of nanotechnologies-enabled autonomous systems capable of replication and of nanotechnologies-enabled human enhancement (e. g. through "intelligent implants") which are seen as "unrealistic" by the scientific community in the foreseeable future. As a consequence, the challenge should be met by the social sciences in the coming years to complement the analysis of the potential disruptive character of nanotechnologies by a differentiated view for nanomedicine where the majority of innovations "in the pipeline" will most likely not be disruptive and revolutionary, but will predominantly lead to stepwise and incremental innovations.

Application of nanotechnologies in the medical sector bears the potential for both health benefits and health risks (see chapter 3.2). The expected health benefits are, together with environmental benefits, the major driver for the very positive attitudes towards nanotechnologies in their entirety prevailing in the general public (chapter 3.12). This high level of the public expectations in nanomedicine forms a certain contrast to the level of public funding devoted to this application area, which, according to estimations of Wagner, Zweck 2005 is in the order of magnitude of 5 % (nanomedicine) to 20 % (life science related nanotechnologies research) of the total nanotechnologies related funding. Findings from surveys, focus groups and citizens' juries point to the importance of transparency in the political decision-making process with respect to the pursued goals and allocation of research funding, to the proactive addressing of potential risks (e. g. from nanoparticles) in research, and call for appropriate forms of involvement of "the public" in this process. In order to realise the potential health benefits, and minimise the health risks, it is required

- to broaden the knowledge base about the health and environmental effects of nanoparticles by high-quality research, and to carry out risk assessments on this basis (see chapter 3.4),
- to take measures (e. g. basic research, development of test schemes, guidance documents, nanotechnologies-specific qualification of staff in regulatory authorities) in order to be able to carry out a dedicated nanotoxicological risk assessment in the frame of market approval of medicinal products and medical devices (see chapter 3.4),
- to strike an appropriate balance in the medicinal products and medical devices market approval process between sufficiently rigid regulatory requirements to ensure safety and quality of the products, but not overly extensive requirements which hinder the access of innovative products to the market,

- to ensure on the one hand that patients have equal access to appropriate diagnostic and therapeutic procedures, among them also nanotechnologies enabled procedures, but to also ensure a just and transparent allocation of scarce health care resources, especially if innovative nanotechnologies-enabled interventions come at higher costs. This requires the integration of health technology assessments and cost-effectiveness studies in the development of these new interventions.

At the present stage of development of the public debate about nanotechnologies, only few non-governmental organisations (NGOs) have developed a position, communicated it and taken a prominent and visible role in the debate in the EU, especially Greenpeace and the etc group. The majority of potentially affected non-governmental organisations<sup>48</sup> in the field of biomedical applications of nanotechnologies are still in an earlier stage of engagement: while the importance and relevance of nanotechnologies and their possible impacts have been acknowledged by many NGOs, the prevailing activity is the monitoring of the development.

Research into the public's attitudes towards nanotechnologies have, so far, only addressed nanotechnologies in their entirety and have not been specifically devoted to nanomedicine. The results obtained so far can be summarised as follows (chapter 3.12): In the general population, there is only a low awareness of nanotechnologies, and very little factual knowledge. Despite specific knowledge, overall assessments of nanotechnologies are positive, and major benefits are anticipated, especially from health and environmental applications of nanotechnologies. However, focus groups and citizens' juries also reveal many aspects which are of concern for the layman, among them mainly how to deal with the inherent uncertainty, and low trust in governmental bodies as well as industry to take decisions for the benefit of the general population. Against this background, there is a high demand for effective regulation and control. In addition, governance issues are stressed and transparency of and public involvement in technology decision-making is called for.

### 3.14 References

Aitken, R.J.; Creely, K.S.; Tran, C.L. (2004): Nanoparticles: An occupational hygiene review, Research Report 274, Sudbury: HSE Books; Health and Safety Executive, Institute of Occupational Medicine.

Allianz; OECD (2005): Opportunities and risks of Nanotechnologies, Lauterwasser, C. (ed.), München, Paris: Allianz; OECD.

---

<sup>48</sup> This relates mainly to consumer organisations, environmental organisations, civil society groups, and industry unions. We are not aware of patient organisations which have genuinely engaged in nanotechnology issues.

- Anderson, A.; Allan, S.; Petersen, A.; Wilkinson, C. (2005): The framing of nanotechnologies in the British newspaper press. In: *Science communication*, 27 (2), pp. 200-220.
- Arnall, A.; Parr, D. (2005): Moving the nanoscience and technology (NST) debate forwards: short-term impacts, long-term uncertainty and the social constitution. In: *Technology in Society*, 27 (1), pp. 23-38.
- Arnall, A.H. (2003): *Future Technologies, Today's Choices. Nanotechnology, Artificial Intelligence and Robotics. A technical, political and institutional map of emerging technologies*, London, UK: Greenpeace Environmental Trust.
- Baber, Z. (2004): "An Undifferentiated Mass of Gray Goo?" *Nanotechnology and Society*. In: *Bulletin of Science, Technology and Society*, 24 (1), pp. 10-12.
- Bainbridge, W.S. (2002): Public attitudes toward nanotechnology. In: *Journal of Nanoparticle Research*, 4 (6), pp. 561-570.
- Baird, D.; Vogt, T. (2004): Societal and Ethical Interactions with Nanotechnology ("SEIN") – An Introduction. In: *Nanotechnology Law & Business*, 1 (4).
- Balshaw, D.M.; Suk, W.A.; Philbert, M. (2005): Research strategies for safety evaluation of nanomaterials, part III: Nanoscale technologies for assessing risk and improving public health. In: *Toxicological Sciences*, 88 (2), pp. 298-306.
- Baumgartner, C. (2004): Ethische Aspekte nanotechnologischer Forschung und Entwicklung in der Medizin. In: *Politik und Zeitgeschichte* (23-24), pp. 39-46.
- Baumgartner, W.; Jäckli, B.; Schmithüsen, B.; Weber, F. (2003): *Nanotechnologie in der Medizin*, TA47/2003, Bern: TA SWISS.
- Berne, R.W. (2004a): Tiny ethics for big challenges: Calling for an ethics of nanoscale and technology. In: *IEEE Circuits and Devices Magazine*, 20 (3), pp. 10-16.
- Berne, R.W. (2004b): Towards the conscientious development of ethical nanotechnology. In: *Science and Engineering Ethics*, 10 (4), pp. 627-638.
- BMRB (2004): *Nanotechnology: Views of the General Public*. BMRB/45/101-666, London, UK: BMRB International Ltd.
- Bock, A.-K.; Rodriguez-Cerezo, E.; Hüsing, B.; Bühlren, B.; Nusser, M. (2005): Human tissue-engineered products: Potential socio-economic impacts of a new European regulatory framework for authorisation, supervision and vigilance. Technical Report EUR 21838 EN. Online: <ftp://ftp.jrc.es/pub/EURdoc/eur21838en.pdf> (Accessed: 17.11.2005).
- Bogedahl, M.; Gleiche, M.; Guibert, J.-C.; Hoffschulz, H.; Locatelli, S.; Malsch, I.; Morrison, M.; Nicollet, C.; Wagner, V. (2003): *Nanotechnology and its Implications for the Health of the EU Citizen, without place*: Nanoforum Consortium.

- Chatterjee, A. (2004): Cosmetic Neurology, The controversy over enhancing movement, mentation and mood. In: *Neurology*, 63, pp. 968-974.
- CIOMS Working Group on Pharmacogenetics (2005): *Pharmacogenetics - Towards improving treatment with medicines*, Shah, R. (ed.), Geneva: Council for International Organizations of Medical Sciences (CIOMS).
- Cobb, M.D. (2005): Framing effects on public opinion about nanotechnology. In: *Science communication*, 27 (2), pp. 221-239.
- Cobb, M.D.; Macoubrie, J. (2004): Public perceptions about nanotechnology: Risks, benefits and trust. In: *Journal of Nanoparticle Research*, 6 (4), pp. 395-405.
- de Jong, W.; Roszek, B.; Geertsma, R.E. (2005): *Nanotechnology in medical applications: possible risks for human health*, RIVM rapport 265001002, Bilthoven, NL: Rijksinstituut voor Volksgezondheid en Milieu (RIVM).
- Dunkley, R.W.S. (2004): Nanotechnology: Social consequences and future implications. In: *Futures*, 36 (10), pp. 1129-1132.
- EGE (2005): *Opinion on Ethical Aspects of ICT Implants in the Human Body*: European Commission, European Group on Ethics in Science and New Technologies (EGE). Online: [http://europa.eu.int/comm/european\\_group\\_ethics/docs/avis20en.pdf](http://europa.eu.int/comm/european_group_ethics/docs/avis20en.pdf) (Accessed: 31.10.2005).
- Einsiedel, E.F.; Goldenberg, L. (2004): Dwarfing the Social? Nanotechnology Lessons From the Biotechnology Front. In: *Bulletin of Science, Technology and Society*, 24 (1), pp. 28-33.
- ETC Group (2003a): *No Small Matter II: The Case for a Global Moratorium - Size Matters!*, Orborne, Canada: Action Group on Erosion, Technology and Concentration (ETC Group).
- ETC Group (2003b): *The Big Down. From Genomes to Atoms*, Orborne, Canada: Action Group on Erosion, Technology and Concentration (ETC Group).
- ETC Group (2004): *Down on the farm: the impact of nano-scale technologies on food and agriculture*, Orborne, Canada: Action Group on Erosion, Technology and Concentration (ETC Group).
- ETC Group (2005a): *NanoGeoPolitics: ETC Group Surveys the Political Landscape*, Communiqué No. 89, Orborne, Canada: Action Group on Erosion, Technology and Concentration (ETC Group).
- ETC Group (2005b): *Nanotech's "Second Nature" Patents: Implications for the Global South*, Communiqués 87 and 88, Orborne, Canada: Action Group on Erosion, Technology and Concentration (ETC Group).
- Faber, B. (2005): *Written popular media representations of nanoscale science & technology, 1986-1999*. Online:

<http://people.clarkson.edu/~faber/pubs/faber.written.media.nanotech.pdf> (Accessed: 13.10.2005).

- Farah, M.J.; Illes, J.; Cook-Deegan, R.; Gardner, H.; Kandel, E.; King, P.; Parens, E.; Sahakian, B.; Wolpe, P.R. (2004): Neurocognitive Enhancement: What Can We Do and What Should We Do? In: *Nature Reviews Neuroscience*, 5 (5), pp. 421-425.
- Farkas, R.; Monfeld, C.; Schmitz-Rode, T.; Appelbe, V.; Schelhaas, U.; Steinbusch, U.; Floren, M.G.; Bremus-Köbberling, E.; Gillner, A.; Klockenbring, T.; Barth, S.; von Zahn, J.; Gothe, H.; Schiffhorst, G.; Reuck, V.; Häussler, B. (2004): *Nanotechnologie pro Gesundheit: Chancen und Risiken*, Aachen: Aachener Gesellschaft für Innovation und Technologietransfer (AGIT).
- Fisher, E. (2005): Lessons learned from the Ethical, Legal and Social Implications program (ELSI): Planning societal implications research for the National Nanotechnology Program. In: *Technology in Society*, 27 (3), pp. 321-328.
- Friedewald, M.; Da Costa, O. (2004): *Science and Technology Roadmapping: Ambient Intelligence in Everyday Life (Aml@Life)*. Summary Report., JRC/IPTS - ESTO Study, Karlsruhe, Seville: Fraunhofer Institute for Systems and Innovation Research (ISI); Institute for Prospective Technological Studies (IPTS); European Science and Technology Observatory.
- Friedewald, M.; Wright, D.; Vildjiounaite, E. (2005): *Safeguards in a World of Ambient Intelligence (SWAMI): Scenario Analysis and Legal Framework - First Results* : Report submitted to the Participants of the First SWAMI Expert Workshop, held in Brussels, 1 June 2005, Karlsruhe: Fraunhofer Institute for Systems and Innovation Research.
- Friele, M.; Fulford, B. (2004): Introduction-intervening in psychic capacities. In: *Poiesis Prax*, 2, pp. 259-262.
- Fuchs, M.; Lanzerath, D.; Hillebrand, I.; Runkel, T.; Balcerak, M.; Schmitz, B. (2002): *Enhancement. Die ethische Diskussion über biomedizinische Verbesserungen des Menschen*, drze-Sachstandsbericht 1, Bonn: Deutsches Referenzzentrum für Ethik in den Biowissenschaften (drze).
- GAEIB (1993): *Opinion on the Ethical Questions Arising from the Commission Proposal for a Council Directive on Legal Protection for Biotechnological Inventions*: European Commission, Group of Advisors on the Ethical Implications of Biotechnology to the European Commission (GAEIB). Online: [http://europa.eu.int/comm/european\\_group\\_ethics/gaieb/en/opinion3.pdf](http://europa.eu.int/comm/european_group_ethics/gaieb/en/opinion3.pdf) (Accessed: 27.10.2005).
- GAEIB (1996): *Ethical Aspects of Patenting Inventions Involving Elements of Human Origin*: European Commission, Group of Advisors on the Ethical Implications of Biotechnology to the European Commission (GAEIB). Online: [http://europa.eu.int/comm/european\\_group\\_ethics/gaieb/en/opinion8.pdf](http://europa.eu.int/comm/european_group_ethics/gaieb/en/opinion8.pdf) (Accessed: 27.10.2005).

- Gaskell, G.; Ten Eyck, T.; Jackson, J.; Veltri, G. (2004): Public attitudes to nanotechnology in Europe and the United States. In: *Nature Materials*, 3 (8), p. 496.
- Gaskell, G.; Ten Eyck, T.; Jackson, J.; Veltri, G. (2005): Imagining nanotechnology: cultural support for technological innovation in Europe and the United States. In: *Public Understanding of Science*, 14 (1), pp. 81-90.
- Gorss, J.B.; Lewenstein, B.V. (2005): The Saliency of Small: Nanotechnology Coverage in the American Press, 1986-2004. Online: <http://www.people.cornell.edu/pages/jbg37/NanoMedialCA2005.pdf> (Accessed: 23.10.2005).
- Grunwald, A. (2005): Nanotechnology - A new field of ethical inquiry? In: *Science and Engineering Ethics*, 11 (2), pp. 187-201.
- Health and Consumer Protection Directorate General of the European Commission (2004): *Nanotechnologies: A preliminary risk analysis on the basis of a workshop organised in Brussels on 1-2 March 2004*, Brussels: European Commission, Health and Consumer Protection Directorate General.
- Hennen, L.; Petermann, T.; Sauter, A. (2000): *Stand und Perspektiven der genetischen Diagnostik. Sachstandsbericht*, Berlin: Büro für Technikfolgen-Abschätzung des Deutschen Bundestages (TAB).
- Hett, A.; Herold, D. (2005): Die Nanotechnologie im Blick der Versicherungswirtschaft. In: *GAIA - Ecological Perspectives for Science and Society*, 14 (1), pp. 24-28.
- Hüsing, B.; Bührlen, B.; Nusser, M. (2004a): *Tissue-engineered products: Potential future socio-economic impacts of a new European regulatory framework*. Unpublished report for IPTS, Karlsruhe: Fraunhofer Institute for Systems and Innovation Research.
- Hüsing, B.; Bührlen, B.; Nusser, M. (2004b): *Tissue-engineered products: Potential future socio-economic impacts of a new European regulatory framework*. Unpublished report for IPTS, Karlsruhe: Fraunhofer Institute for Systems and Innovation Research.
- Hüsing, B.; Engels, E.-M.; Frietsch, R.; Gaisser, S.; Menrad, K.; Rubin, B.; Schubert, L.; Schweizer, R.; Zimmer, R. (2003): *Menschliche Stammzellen*, TA44/2003, Bern: Zentrum für Technologiefolgen-Abschätzung, TA SWISS.
- Hüsing, B.; Engels, E.-M.; Gaisser, S.; Zimmer, R. (2001): *Zelluläre Xenotransplantation*, TA 39/2001, Bern: Zentrum für Technologiefolgen-Abschätzung beim Schweizerischen Wissenschafts- und Technologierat.
- Hüsing, B.; Jäncke, L.; Tag, B. (2005): *Impact Assessment of Neuroimaging*. Still unpublished draft final report TA-SWISS xx/2006, Bern, Switzerland: Centre for Technology Assessment at the Swiss Science and Technology Council (TA-SWISS).

- Hüsing, B.; Menrad, K.; Menrad, M.; Scheef, G. (1999): Functional Food - Funktionelle Lebensmittel. TAB-Hintergrundpapier Nr. 4, Berlin: Büro für Technikfolgen-Abschätzung beim Deutschen Bundestag (TAB).
- Hüsing, B.; Schicktanz, S. (2000): Bestandsaufnahme von aktuellen FuE-Aktivitäten und -Trends auf dem Gebiet der Xenotransplantation von Organen, Karlsruhe: Fraunhofer-Institut für Systemtechnik und Innovationsforschung.
- Ibarreta, D.; Elles, R.; Cassiman, J.-J.; Rodriguez-Cerezo, E.; Dequeker, E. (2004): Towards quality assurance and harmonization of genetic testing services in the European Union. In: *Nat Biotech*, 22 (10), pp. 1230-1235.
- Illes, J.; Raffin, T.A.; Huang, L.; Goldstein, R.A.; Atlas, S.W.; Rosen, A.C.; Swan, G. (2004): Ethical consideration of incidental findings on adult brain MRI in research. In: *Neurology*, 62 (6), pp. 888-890.
- Illes, J.; Desmond, J.E.; Huang, L.F.; Raffin, T.A.; Atlas, S.W. (2002): Ethical and practical considerations in managing incidental findings in functional magnetic resonance imaging. In: *Brain and Cognition*, 50 (3), pp. 358-365.
- Invernizzi, N.; Foladori, G. (2005): Nanotechnology and the Developing World: Will Nanotechnology Overcome Poverty or Widen Disparities? In: *Nanotechnology Law & Business*, 2 (3), pp. 1-10, Article 11.
- Jain, K.K. (2005): The role of nanobiotechnology in drug discovery. In: *Drug Discovery Today*, 10 (21), pp. 1435-1442.
- Katz, E.; Lovel, L.; Mee, W.; Solomon, F. (2005): Citizens' Panel on Nanotechnology. Report to Participants, Report DMR-2673, Melbourne, Australia: CSIRO Minerals.
- Kennedy, D. (2004): Just Treat, or Enhance? In: *Science*, 304 (5667), p. 17.
- Kleinman, D.; Powell, M. (2005): Report of the Madison Area Citizen Consensus Conference on Nanotechnology, Madison: Initiative on Nanotechnology and Society, University of Wisconsin.
- Kollek, R.; Feuerstein, G.; Schmedders, M.; van Aken, J. (2004): Pharmakogenetik: Implikationen für Patienten und Gesundheitswesen, Baden-Baden: Nomos.
- komm.passion GmbH (2004): Wissen und Einstellung zur Nanotechnologie - Höchste Zeit die Weichen zu stellen, Düsseldorf: komm.passion GmbH.
- Laurent, L.; Petit, J.-C. (2005): Nanosciences and its Convergence with other Technologies. New Golden Age or Apocalypse? In: *HYLE - International Journal for Philosophy of Chemistry*, 11 (1), pp. 45-76.
- Lee, C.J.; Scheufele, D.A.; Lewenstein, B.V. (2005): Public attitudes toward emerging technologies: Examining the interactive effects of cognitions and affect on public attitudes toward nanotechnology. In: *Science communication*, 27 (2), pp. 240-267.

- Lewenstein, B.V. (2005): What Counts as a "Social and Ethical Issue" in Nanotechnology? In: HYLE - International Journal for Philosophy of Chemistry, 11 (1), pp. 5-18.
- Lloyd, S.M.; Lave, L.B. (2003): Life cycle economic and environmental implications of using nanocomposites in automobiles. In: Environmental Science and Technology, 37 (15), pp. 3458-3466.
- Lloyd, S.M.; Lave, L.B.; Matthews, H.S. (2005): Life cycle benefits of using nanotechnology to stabilize platinum-group metal particles in automotive catalysts. In: Environmental Science and Technology, 39 (5), pp. 1384-1392.
- Löchtefeld, S.; Kühr, A.-K.; Claus, F. (2005a): Synthetische Nanopartikel. Blick auf Umwelt- und Gesundheitsaspekte. Im Auftrag des Umweltbundesamtes, Förderkennzeichen 205 61 220, Dortmund: iku GmbH.
- Löchtefeld, S.; Kühr, A.-K.; Claus, F. (2005b): Synthetische Nanopartikel. Ergebnisse der Stakeholderbefragung. Im Auftrag des Umweltbundesamtes. Förderkennzeichen 205 61 220, Dortmund: iku GmbH.
- Lopez, J. (2004): Compiling the ethical, legal and social implications of nanotechnology. In: Health Law Rev, 12 (3), pp. 24-27.
- Luther, W.; (ed) (2004): Industrial applications of nanomaterials - chances and risks. Technology analysis, Future Technologies No. 54, Düsseldorf: Future Technologies Division of VDI Technologiezentrum GmbH.
- MacDonald, C. (2004): Nanotech is Novel; the Ethical Issues Are Not. In: Scientist, 18 (3), p. 8.
- Macnaghten, P.; Kearnes, M.B.; Wynne, B. (2005): Nanotechnology, governance, and public deliberation: What role for the social sciences? In: Science communication, 27 (2), pp. 268-291.
- Macoubrie, J. (2005): Informed Public Perceptions of Nanotechnology and Trust in Government. Project on Emerging Nanotechnologies, Washington DC: Woodrow Wilson International Center for Scholars, The Pew Charitable Trust.
- Macoubrie, J. (2006): Nanotechnology: public concerns, reasoning and trust in government. In: Public Understanding of Science, 15 (2), pp. 221-241.
- Malsch, I.; Gleiche, M.; Hoffschulz, H.; Locatelli, S.; Nicollet, C.; Guibert, J.-C.; Bogedahl, M.; Morrison, M.; Oud, M. (2004): Benefits, Risks, Ethical, Legal and Social Aspects of Nanotechnology, Nanoforum General Report on Nanotechnology in Europe No. 4, without place: Nanoforum Consortium.
- Mark, D. (2005): Nanomaterials - a risk to health at work? First International Symposium on Occupational Health Implications of Nanomaterials, 12-14 October 2004, Buxton: Health and Safety Executive; National Institute for Occupational Safety and Health.

- Marris, C.; Wynne, B.; Simmons, P.; Weldon, S. (2001): Public Perceptions of Agricultural Biotechnologies in Europe. Final Report of the PABE research project, funded by the European Commission, contract number FAIR CT98-3844, Lancaster: Centre for the Study of Environmental Change, Lancaster University.
- Matsuura, J. (2004): Expecting the public backlash: Public relations lessons for nanotechnology from the biotechnology experience. In: 2004 NSTI Nanotechnology Conference and Trade Show - NSTI Nanotech 2004, 3, pp. 491-493.
- McGuire, G.Q.; McGee, E.M. (1999): Implantable brain chips? Time for debate. In: Hastings Center Report, 29 (1), pp. 7-13.
- Mehta, M.D. (2004): From Biotechnology to Nanotechnology: What Can We Learn From Earlier Technologies? In: Bulletin of Science, Technology and Society, 24 (1), pp. 34-39.
- Menrad, M.; Hüsing, B.; Menrad, K.; Reiß, T.; Beer-Borst, S.; Zenger, C.A. (2000): Functional Food. TA 37/2000, Bern: Zentrum für Technologiefolgen-Abschätzung beim Schweizerischen Wissenschafts- und Technologierat.
- Mnyusiwalla, A.; Daar, A.S.; Singer, P.A. (2003): 'Mind the gap': Science and ethics in nanotechnology. In: Nanotechnology, 14 (3), p. R9-R13.
- Monk, R.; Rachamim, A. (2005): Research Training in Nanosciences and Nanotechnologies: Current Status and Future Needs. Proceedings of the workshop held in Brussels, 14-15 April 2005, Brussels: European Commission, Directorate-General for Research, Unit G.4 Nanosciences and Nanotechnologies.
- Munich Re Group (2002): Nanotechnology - what is in the store for us?, Munich: Munich Re Group.
- National Science Foundation (2002): Converging technologies for improving human performance - Nanotechnology, biotechnology, information technology and cognitive science., Roco, M.C.; Bainbridge, W.S. (eds.), Washington DC: National Science Foundation.
- Parr, D. (2005): Will nanotechnology make the world a better place? In: Trends in Biotechnology, 23 (8), pp. 395-398.
- Paschen, H.; Coenen, C.; Fleischer, T.; Grünwald, R.; Oertel, D.; Revermann, C. (2003): TA-Projekt Nanotechnologie. Endbericht, Berlin: Büro für Technikfolgen-Abschätzung beim Deutschen Bundestag.
- Pauen, M. (2004): Illusion Freiheit? Mögliche und unmögliche Konsequenzen der Hirnforschung, Frankfurt/M.: S. Fischer.
- Präsident der Berlin-Brandenburgischen Akademie der Wissenschaften (2004): Zur Freiheit des Willens. Streitgespräch in der Wissenschaftlichen Sitzung der Versammlung der Berlin-Brandenburgischen Akademie der Wissenschaften am 27. Juni 2003, Debatte, Berlin: Berlin-Brandenburgische Akademie der Wissenschaften.

- Priest, S.H. (2005): Commentary - Room at the bottom of pandora's box: Peril and promise in communicating nanotechnology. In: *Science communication*, 27 (2), pp. 292-299.
- Raeymaekers, P.; Rondia, K.; Slob, M. (2004): *Connecting Brains and Society. The present and future of brain science - what is possible, what is desirable?* International Workshop, 22 and 23 April 2004, Amsterdam, the Netherlands. Proceedings and synthesis report, Brussels, The Hague: King Baudouin Foundation, Rathenau Institute.
- Roco, M.C. (2003a): Broader societal issues of nanotechnology. In: *Journal of Nanoparticle Research*, 5 (3-4), pp. 181-189.
- Roco, M. (2003b): Nanotechnology: convergence with modern biology and medicine. In: *Current Opinion in Biotechnology*, 14 (3), pp. 337-346.
- Rohr, M.; Schade, D. (2000): *Selbstbestimmung und Eigenverantwortung im Gesundheitswesen*, Stuttgart: Akademie für Technikfolgenabschätzung in Baden-Württemberg.
- Roth, G. (2001): *Willensfreiheit und Autonomie - Fühlen, Denken, Handeln. Wie das Gehirn unser Verhalten steuert*, Roth, G. (ed.), Frankfurt/M.: Suhrkamp Verlag, pp. 427-449.
- SCENIHR (2005): *Opinion on The appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies*, Brussels: European Commission, Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). Online: [http://europa.eu.int/comm/health/ph\\_risk/committees/04\\_scenihr/docs/scenihr\\_o\\_003.pdf](http://europa.eu.int/comm/health/ph_risk/committees/04_scenihr/docs/scenihr_o_003.pdf) (Accessed: 25.10.2005).
- Scheufele, D.A.; Lewenstein, B.V. (2005): The public and nanotechnology: How citizens make sense of emerging technologies. In: *Journal of Nanoparticle Research*, 7 (6), pp. 659-667.
- Schummer, J. (2004): *Societal and Ethical Implications of Nanotechnology: Meanings, Interest Groups, and Social Dynamics*. In: *Techné: Research in Philosophy and Technology*, 8 (2), pp. 1-29.
- Schummer, J. (2005): Reading nano: the public interest in nanotechnology as reflected in purchase patterns of books. In: *Public Understanding of Science*, 14 (2), pp. 163-183.
- Sheetz, T.; Vidal, J.; Pearson, T.D.; Lozano, K. (2005): Nanotechnology: Awareness and societal concerns. In: *Technology in Society*, 27 (3), pp. 329-345.
- Sheremeta, L. (2004): Nanotechnology and the ethical conduct of research involving human subjects. In: *Health Law Rev*, 12 (3), pp. 47-56.

- Sheremeta, L.; Daar, A.S. (2004): The case for publicly funded research on the ethical, environmental, economic, legal and social issues raised by nanoscience and nanotechnology (NE3LS). In: *Health Law Rev*, 12 (3), pp. 74-77.
- Singer, W. (2003): *Das Ende des freien Willens? - Ein neues Menschenbild? Gespräche über Hirnforschung*: Suhrkamp Taschenbuch wissenschaft, pp. 24-34.
- Steinfeldt, M.; von Gleich, A.; Petschow, U.; Haum, R.; Chudoba, T.; Haubold, S. (2004): *Nachhaltigkeitseffekte durch Herstellung und Anwendung nanotechnologischer Produkte*, Schriftenreihe des IÖW 177/04, Berlin: Institut für ökologische Wirtschaftsforschung gGmbH.
- Stephens, L.F. (2005): News narratives about nano S&T in major U.S. and non-U.S. newspapers. In: *Science communication*, 27 (2), pp. 175-199.
- Stephens, L.F.; McKissick, J.R. (2004): *News Narratives about Nano: How Journalists and the News Media Are Framing Nanoscience and Nanotechnology Initiatives and Issues*. Presentation at the Imaging and Imagining Nanoscience & Engineering Conference, University of South Carolina, Columbia, SC, March 4-7, 2004. Online: <http://129.252.169.87/rstephens/stephensnanomsUSCMar04.pdf> (Accessed: 13.10.2005).
- Stipkala, J.M. (2005): Overcoming obviousness when patenting nanotechnology inventions. In: *Nat Biotech*, 23 (6), pp. 677-678.
- Sweeney, A.E.; Seal, S.; Vaidyanathan, P. (2003): The promises and perils of nanoscience and nanotechnology: Exploring emerging social and ethical issues. In: *Bulletin of Science, Technology and Society*, 23 (4), pp. 236-245.
- Swiss Re (2004): *Nanotechnology. Small matter, many unknowns*, Hett, A. (ed.), Zurich: Swiss Reinsurance Company.
- The Royal Society (2005): *Personalised medicines: hopes and realities*, London: The Royal Society.
- The Royal Society & The Royal Academy of Engineering (2004): *Nanoscience and nanotechnologies: opportunities and uncertainties*, London: The Royal Society.
- Tomellini, R.; de Villepin, C. (2005): *Research Needs on Nanoparticles*. Proceedings of the Workshop held in Brussels 25-26 January 2005, Brussels: European Commission, Directorate-General for Research.
- Toumey, C. (2004): Nano Hyperbole and Lessons from Earlier Technologies. In: *Nanotechnology Law & Business*, 1 (4), pp. 397-405.
- Türk, V.; Kaiser, C.; Liedtke, C.; Vedder, D.; Kastenholz, H.; Köhler, A.; Knowles, H.; Murray, V. (2005a): *Nanologue Background Paper on selected nanotechnology applications and their ethical, legal and social implications*, Wuppertal: Wuppertal Institute; EMPA; Forum for the Future; triple innova.

- Türk, V.; Steger, S.; Liedtke, C.; Kastenholz, H.; Köhler, A.; Knowles, H.; Aldrich, T.; Kuhndt, M.; Schaller, S. (2005b): Nanologue Mapping Study. Summary of key findings from a literature study on ethical, legal and social aspects of nanotechnologies., Wuppertal: Wuppertal Institute; EMPA; Forum for the Future; triple innova.
- Wagner, V.; Zweck, A. (2005): Nanobiotechnology in the medical sector - Drivers for development and possible impacts. Confidential report for WP1 (Current status of nanobiotechnology for medical applications in Europe) and WP2 (Identification of the main drivers and challenges for medicinal nanobiotechnology and its impact on the medical sector), Düsseldorf: Zukünftige Technologien Consulting.
- Wegner, D.M. (2002): *The Illusion of Conscious Will*, Cambridge, MA: Bradford Books.
- Weil, V. (2003): Zeroing in on ethical issues in nanotechnology. In: *Proceedings of the IEEE*, 91 (11), pp. 1976-1979.
- Wiedemann, P.M.; Schütz, H. (2005): *Risikowahrnehmung der Nanotechnologie: Eine experimentelle Studie*, 90, Jülich: Programmgruppe Mensch, Umwelt, Technik; Forschungszentrum Jülich.
- Wolpe, P.R. (2002): Treatment, enhancement, and the ethics of neurotherapeutics. In: *Brain and Cognition*, 50 (3), pp. 387-395.
- Wood, S.; Jones, R.; Geldart, A. (2005): *The Social and Economic Challenges of Nanotechnology*, Swindon: Economic and Social Research Council (ESRC).

## 4 Annex

### 4.1 Email survey, conducted for chapter 2

The following e-mail was sent to a total of 25 experts:

Dear Professor [name],

On behalf of the EU and the Institute for Prospective Technological Studies (IPTS) we conduct a study on nanobiotechnology in the medical sector.

We would like to evaluate the impact of nanobiotechnology on health care costs.

In order to put the German results analyzed by Farkas et al 2004 in the European context I would like to ask you to comment on the following six theses and questions from the [insert country of expert] and European perspective.

1. The cost drivers in the health system are the following MDC: neoplasms, cardiovascular disease, diseases of the nervous system, musculo-skeletal disease.
2. Disease groups that contribute significantly to the total days in hospital (inpatient care) are:  
neoplasms, psychiatric diseases, cardiovascular diseases
3. Technology dependent costs account for a maximum of 20 % of the total costs. Thus nanotechnological innovations can have only a significant impact on health costs if they reduce personnel costs by reduction of the number of days in hospital.
4. In detail nanotechnology will impact health expenditures as follows:
  - Cardiovascular disease (including stroke) and neurodegenerative disease: no significant potential for cost reduction, cost drivers are intensive care for chronic patients and rehabilitation of stroke patients.
  - Neoplasms: potential for some cost savings by early screening and prevention. However, add on innovations of conventional chemotherapeutic drugs will result in higher costs.
  - Musculoskeletal diseases: small effect, as prosthesis with longer lifespan do not play an important role for the (older) recipients of endoprotheses.
  - The development of combined therapeutic approaches (combination of diagnosis and therapy; personalized medicine) will give significant impetus for innovations activities.

5. Apart from the technological improvement future framework for approval and reimbursement are key issues for the impact of nanotechnology on the health system.

6. Finally I would like to ask you for further information:

- Which nanotechnological innovations will impact the health care costs in your opinion?
- Do you know relevant cost analyses of nanotechnological studies for the medical sector? (So far we identified comprehensive information about liposomal Amphotericin B (AmBisome) and pegylated doxorubicin).

7. Comments?

Thank you very much for your help. If you would like further information please contact me via phone (+49/(0) 721-68 09 205) or email ([s.gaisser@isi.fraunhofer.de](mailto:s.gaisser@isi.fraunhofer.de)). I would be very happy if you could send your reply until 14th of October 2005.

Kind regards

Dr. Sibylle Gaisser

## 4.2 Health economics experts contacted in the frame of the email survey in chapter 2

Name	Institution	Country	Commented results
P. Leclercq	Dep. de Economie de la Santé, Université libre de Brussel	BE	no
Prof. Peter Zweifel	Socioeconomic Institute, University of Zurich	CH	yes
Prof. Bernard Jeune	Institute of Public Health, University of Southern Denmark	DK	no
F. Guillemin	Ecole du Santé Public, Université de Nancy	FR	no
R. Salamon	Department d'informacion medicale, Université de Bordeaux	FR	no
S. Briancon	Ecole de Santé Public, Université de Nancy	FR	no
Dr. Samantha Smith	Trinity College Dublin	IRL	yes
Prof. Miriam Wiley	The Economic and Social Research Institute, ESRI	IRL	no

Name	Institution	Country	Commented results
Dr. Michael Barry	Economist at St. James' Hospital, Dublin	IRL	no
Dr. Stefano Capri	Institute for Economy, University Carlo Cattaneo-LIUC	IT	yes
Prof. Pieter Kramers	National Institute for Public Health and Environment	NL	yes
Prof. Frans Rutten	Institute for Medical Technology Assessment, Erasmus University, Rotterdam	NL	no
Prof. Grete Botten	Institute for Health Management and Health Economics, University of Oslo	No	no
Prof. Jan E. Askildsen	Department of Economics, University of Bergen	No	no
Prof. Terje P. Hagen	Institute for Health Economy, University of Oslo	No	no
Prof. Björn Lindgren	Centre for Health Economics, Lund University	SE	no
Prof. Carl H. Lyttkens	Department of Economics, Lund University	SE	no
Prof. Gill Walt	Institute for Health Policy, University of London	UK	no
Prof. Robin Milne	Department of Economics, University of Glasgow	UK	no
T. Kirkwood	Institute for Ageing and Health, University of Newcastle	UK	no
F. Noorbakhsh	Department of Economics, University of Glasgow	UK	no
I.K. Crombie	Institute for Epidemiology and Public Health, University of Dundee	UK	no
J. Edwardson	Institute for Ageing and Health, University of Newcastle	UK	no
M. Drummond	Centre for Health Economics, University of York	UK	no
R. Zimmern	Public Health Genetics Unit, University of Cambridge	UK	no

### 4.3 Experts interviewed for chapter 3

Dr. Donald Bruce, Society, Religion and Technology Project, Church of Scotland, Edinburgh, Scotland

Dr. Wolfgang Dubbert, Scientist in charge of nanotechnology, Federal Environmental Agency, Berlin, Germany

Dr. Angela Hullmann, European Commission, DG Research, Brussels, Belgium

Dr. Hans G. Kastenholz, Technology and Society Lab, Head of Unit, Innovation and Technology Analysis, Swiss Federal Laboratories for Materials Testing and Research (EMPA), St. Gallen, Switzerland

Ulrich Klotz, Department Economy, Technology, Environment, Management Board, IG Metall (Metal Trade Union), Frankfurt/M., Germany

Christoph Lauterwasser, Allianz Center for Technology GmbH, Ismaning, Germany

Dr. Christoph Meili, Die Innovationsgesellschaft mbH, St. Gallen, Switzerland

Doug Parr, Chief Scientist, in charge of nanotechnology, Greenpeace UK, London, UK

Dr. Tilo Propp, Department of Business, Public Administration and Technology, University of Twente, Enschede, The Netherlands

Prof. Dr. Arie Rip, Professor of Philosophy of Science and Technology, Department of Business, Public Administration and Technology, University of Twente, Enschede, The Netherlands

Volker Türk, Wuppertal Institute, Sustainable Production and Consumption Department, Wuppertal, Germany

Iris Wolf, Head of Department Research – Technology, Industriegewerkschaft Bergbau, Chemie, Energie (Mining, Chemical and Energy Industrial Union), Hannover, Germany

Dr. René Zimmer, Department 22 (Risk Perception and Early Warning), Bundesinstitut für Risikobewertung (Federal Institute for Risk Assessment), Berlin, Germany