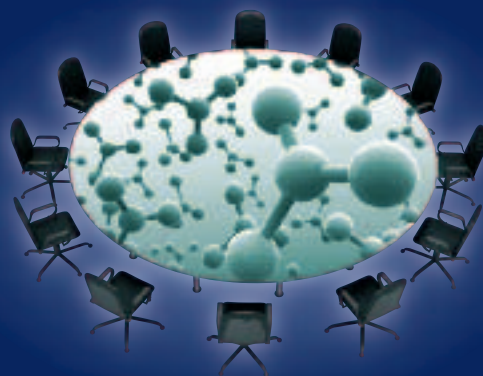


A report on the nanomedicine environment

ECONOMIC
REGULATORY
ETHICAL & SOCIAL
PATIENTS
PUBLIC COMMUNICATION



NanoMed Round Table Extended Report



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Overview

Nanomedicine is the application of nanotechnology in medicine and healthcare, at the molecular level. To put this in context, the molecules in our bodies and the structures inside our cells operate at the scale of about 100 nanometres or less - a nanometre is one-billionth of a metre.

Although very promising, nanomedicine may add new dimensions to many ethical, societal and economic issues. For the promises to be realised and to achieve the maximum benefit of nanomedical innovations for everyone, the way has to be paved for a safe, integrated and responsible approach to nanomedicine. This will also be a necessary condition for the sustainable competitiveness of nanomedical research and development in Europe, and of its healthcare industry. It is therefore of primary importance to understand the possible impacts and consequences of nanomedicine in advance.

The NanoMed Round Table brought together expert stakeholders from across Europe within five Working Groups, each of which considered a specific field highly relevant to decision-making regarding nanomedical innovations.

The Groups' key findings were as follows:

- **Patients' Needs** – Our research shows that patients want nanomedicine and they want to know more about it from reliable sources. The European Commission, national governments, and trade and research associations all have a role to play in ensuring dialogue with, and information provision to, patients.
- **Ethical and Societal Aspects** - Ethical engagement with nanomedicine needs to begin with the very concept of 'nanomedicine', a word that now groups diverse research activities together. Nanomedical researchers, physicians, patients, and policy makers will all benefit when, on the basis of philosophical and social analysis, the programme and purpose of nanomedicine are better understood and more clearly defined.
- **Economic Impact** - Reliable data is needed to predict the impact of nanomedicine on healthcare costs and benefits, and market growth. This information is required to enable the EMEA to make decisions on early interventions and national authorities to make reimbursement decisions.
- **Regulation** - A proactive regulatory system is required that ensures better coordination and harmonisation of regulatory procedures, early dialogue with users and stakeholders, and takes account of the economic cost implications of regulation. Given its recently enhanced role, it seems reasonable to suggest that DG SANCO should take the lead in encouraging European level regulatory bodies to achieve this aim. At Member State level, national governments should encourage national regulatory bodies to take similar action.
- **Communication** – The European Commission should provide credible and accessible sources of balanced information about nanomedicine, to facilitate understanding and dialogue.

Nanomedical applications are not just a theoretical possibility – for example, the Round Table has identified forty-five products that are already on the market. However, the field of nanomedicine is still a relatively new one. This means that as this report is published, Europe is at an ideal moment to consider the impacts and consequences of nanomedicine, as well as action required as a result.

Several factors serve to underline the particular relevance and timeliness of this report. The recently enhanced role of DG SANCO, and the European Commission's anticipated strategic Action Plan for Nanosciences and Nanotechnologies 2010-2015, rank among these. Another factor is the scale and depth of impact that nanomedicine may deliver, which should not be underestimated. Nanomedicine is enabling us to take a significant step forward in understanding and treating disease, by shifting attention to the molecular level.

As well as adding another layer to healthcare, nanomedicine also presents us with arguably the best case study of changing business models in terms of the move from curative to preventive medicine. In the context of health being viewed increasingly as 'well-being' rather than 'absence of disease', nanomedicine may have much to contribute.

Nanomedicine is also covering new ground in that it is combining many previously unconnected disciplines, such as economics, supply chain and insurance, to name but a few. This convergence of different fields means that we need to be very clear about where and how we start thinking about the impact of nanomedicine.

For all of these reasons, not taking action now would be a wasted opportunity. By doing nothing, we would significantly risk blocking the development of innovative procedures in Europe, to the detriment of European research and development, the healthcare industry, and, most importantly, patients.

It's never too early to act until it's too late.

¹ US National Institutes of Health: <http://nihroadmap.nih.gov/nanomedicine>

² The European Medicines Agency, whose "main responsibility is the protection and promotion of public and animal health, through the evaluation and supervision of medicines for human and veterinary use": www.ema.europa.eu

³ The European Commission Directorate General for Health and Consumers

* Ref. Economic Impact Working Group

Summary of Recommendations

Communication and Dialogue About Nanomedicine

The European Commission should:

- establish a platform to provide credible and accessible sources of balanced information on the methods, benefits and risks of nanomedicine.
- investigate funding opportunities for EU level trade and research associations to produce lay information using stakeholder dialogue on nanomedicine research.
- support patient organisations to investigate whether nanomedicine is currently/potentially useful in treating their condition (with a view to their providing balanced information to patients if so), and provide funding to identify and understand the issues that it raises for them.
- develop communication guidelines for the various nanomedicine stakeholders, and provide good practice examples.

The European Commission, national governments, industry and independent grant organisations should allocate a significant percentage of financial resources in the field of nanomedicine to public communication.

The European Commission and national funding agencies should integrate public involvement in decision making on priorities in research funding and encourage, train and reward scientists in public engagement activities.

Patient organisations should be involved in the work of the European Technology Platform on Nanomedicine and the “NANO futures” European Technology Integration and Innovation Platform in Nanotechnology initiative, and be encouraged to participate in governmental stakeholder fora. Patients’ involvement in EU and national policy making processes should also be institutionalised.

Parliamentarians at EU and national level should conduct multi-stakeholder hearings, to deliberate in a comparative manner the value of basic nanomedical research for prevention, diagnosis and therapy of disease.

The Potential and Implications of Nanomedicine

The European Commission and national governments should:

- integrate the deliberation of ethical and societal issues with consideration of the feasibility of particular developments in nanomedicine.
- encourage social science and humanities research that goes beyond the risks and benefits of medical innovations to include the consideration of promises, hopes and anxieties.
- support the development of a broader range of methodologies for research on the environmental, health and social implications, and on the ethical, legal and social aspects, of nanomedicine.

Promoting Nanomedicine Research

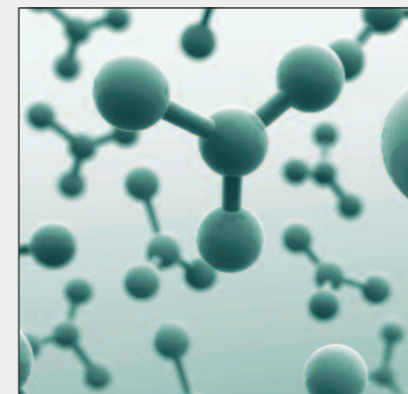
The European Commission and national governments should:

- together with the European Science Foundation and the European Research Council, initiate a deliberative process about the possibly distinctive features of nanomedicine that include its social and ethical dimensions. This process should inform the setting of EU Framework Programme and national research agendas.
- in consultation with patient organisations, continue to discuss priorities for nanomedicine and fund their research and development, encouraging the integration of national nanomedicine strategies to ensure complementarity.
- establish partially public-funded technology-specific reference centres linking early development with clinical research and clinical practice.

Ensuring a Supportive Regulatory Environment for Nanomedicine

The European Commission should:

- establish and promote supporting mechanisms that boost the effectiveness of the existing regulatory framework, especially by harmonising regulatory procedures on reporting and data collection.
- ensure the proportionate responsiveness of regulatory policies through engagement and partnership with users and stakeholders, as well as taking into account factors that differ between Member States (e.g. national regulatory infrastructures and cultures), and monitoring health and environmental impact.
- support institutional mechanisms that facilitate a common perspective regarding clarity, objectivity and common practice for credibility and authority.
- regulators should take into consideration the economic implications of regulation for nanomedicine and the funding support needed for access to regulatory expertise and extra compliance investment, especially for SMEs.



Nanomedicine in Healthcare Systems

Companies and clinicians should produce data based on well-defined criteria of cost-effectiveness for the economic evaluation of nanotechnology-based innovations in clinical trials and health technology assessment studies.

The European Commission should:

- together with national governments, promote and support projects in partnership with key stakeholders, to assess the cost-effectiveness of nanomedical innovations as early as possible.
- launch a health economics project to assess the economic impact and emergence of new cost models relating to nanotechnological innovations in preventive medicine and the monitoring of chronic diseases..
- provide funding to examine access issues relating to nanomedicine products.
- support further research to work with bodies representing clinicians to gauge awareness of novel possibilities arising from nanomedicine and incorporate these into clinical practice.
- national reimbursement agencies and public and private insurers should establish a European working group to consider the future impact of innovative approaches in healthcare systems with nanotechnology as a case study.

Nanomedicine in a Global Context

The European Commission should:

- to improve European and international strategies for maximising the positive economic impact of nanomedicine.
- together with national governments, involve low-income countries in developing a fair and sustainable global policy on benefit sharing in nanomedicine.

Patient Views and Understanding of Nanomedicine

A Report by the Patients' Needs Working Group of the NanoMed Round Table

Summary and Recommendations

KEY POINTS

Patients have relatively low levels of knowledge and awareness of nanomedicine, but they would like more information.

Despite this low level of knowledge there are high levels of support among patients for nanomedicine products and research.

Patients have clear views on how and from whom they would like to receive this information.

Patients do not think that nanomedicine is inherently unsafe, but there is a lack of clear understanding about the potential safety aspects.

Nanomedicine is an opportunity that patients want to see embraced. Equally, there is a significant and time-critical opportunity to inform patients about it.



Patients' Awareness of Nanomedicine

There is low awareness and knowledge of nanomedicine among patients and patient organisations, even in condition areas where it is being used. The overwhelming majority of patients would like to receive more information on nanomedicine, ideally via the internet, from patient organisations and/or clinicians.

Recommendation 1

The European Technology Platform on Nanomedicine and "NANO futures" European Technology Integration and Innovation Platform in Nanotechnology, together with the European Patients' Forum, should explore the involvement of patient organisations in the work of the Platforms, to provide input from patients' perspective and improve patients' understanding of nanomedicine. For these reasons, patient organisations' views should also actively be sought as part of any other nanomedicine strategy development at EU level.

Recommendation 2

The European Commission has produced much useful information on the internet on nanotechnology aimed at the general public, e.g. short films, leaflets and brochures. It should organise the production of similar lay information on nanomedicine, which could be used by patient organisations, clinicians and the media.

Recommendation 3

European-level trade and research associations should produce lay information using stakeholder dialogue on nanomedicine research. National-level trade and research associations should disseminate this information in their country's language(s) to patient organisations, media and

bodies representing clinicians. The European Commission should investigate what existing programmes should or could fund this, and/or develop new funding streams where required, e.g. science and society programmes or European Science Foundation.

Recommendation 4

Patient organisations should be supported by the European Commission to investigate whether nanomedicine is currently or potentially useful in treating their condition, and if so to enable engagement in nanomedicine with a view to providing balanced information to patients and carers.

Recommendation 5

The European Commission, working with the European Patients' Forum, should identify and engage with patient organisations that already communicate to their members on nanomedicine, and work with them to produce a 'best practice' case study and toolkit (e.g. FAQs, webpages, short files) to help guide and support other patient organisations.

Patient Support for Nanomedicine

The majority of patients view nanomedicine as a technology that could address many unmet medical needs and they support nanomedicine research.

Recommendation 6

The European Commission and national governments in consultation with patient organisations should continue to discuss priorities for nanomedicine and fund their research and development. To ensure complementarity and avoid duplication, the European Commission should encourage the integration of national nanomedicine strategies.

Safety and Risk

Patients do not view nanomedicine as inherently unsafe, but there is a lack of clear understanding about the potential safety aspects that may be unique to it. This should be addressed through appropriate safeguards and the communication of information. Patients have mixed views on whether nanomedicine is different from other new types of medical research.

Recommendation 7

Where governments have organised stakeholder fora to discuss the potential risks and benefits of nanotechnologies including nanomedicine, they should encourage patient organisations to participate. Where such fora do not exist, governments should urgently consider establishing them.

Recommendation 8

The European Commission should provide funding for focus groups and other participatory methods (e.g. citizen conferences, interviews, surveys) in a number of European countries, to identify and understand the spectrum of issues that nanomedicine raises for patients and their families.

Access and Clinical Preparedness

Further research is desirable on access to nanomedicine products and clinical preparedness.

Recommendation 9

The European Commission should provide funding for a project examining access issues relating to nanomedicine products (diagnostic and therapeutic).

Recommendation 10

The European Commission should support further research to work with bodies representing clinicians and other healthcare professionals to: a) gauge awareness of novel possibilities arising from nanomedicine and incorporate these into clinical practice, and b) assist CPD/CME (Continuous Professional Development/Continuing Medical Education) to anticipate novel possibilities and formulate appropriate responses.

Patients' Awareness and Knowledge of Nanomedicine

The findings of this pilot study are based on the results of research undertaken between June and September 2009. This consisted of an online questionnaire, to which 87 people responded, 12 interviews conducted face-to-face or by telephone and one focus group held with the West Cumbria branch of the Parkinson's Disease Society, which was attended by 17 Parkinson's patients and carers.

i. Current Levels of Awareness

As the European Commission states: "(n)anomedicine, the application of nanotechnology to health, raises high expectations for millions of patients for better, more efficient and affordable healthcare and has the potential of delivering promising solutions to many illnesses." In view of this, arguably the most notable finding from the research conducted by the Patients' Needs Working Group was the low level of awareness and knowledge among patients and patient organisations of nanomedicine and its uses. It is possible that the people who took part in the research were more informed than average, but awareness and knowledge were nonetheless low.

¹ <http://cordis.europa.eu/nanotechnology/nanomedicine.htm#challenge>

² This varied by type of respondent, from around 70 per cent of the patient organisation leaders (8 out of 11), half of the patients who responded and none of the carers/relatives who responded to that question.

Two-thirds of interviewees had never heard of nanomedicine, whereas the remainder had heard of it but had not realised until the interview that it was nanomedicine. Furthermore, **over half of the interviewees and 52 out of 85 online survey respondents had not heard of any use of nanomedicine in their particular condition areas.** This could be attributed to straightforward lack of awareness of current nanomedicine research and development. On the other hand, it could be because nanomedicine is not yet being used in many condition areas.

Parkinson's Disease is one condition where nanomedicine is already in use, so one might expect awareness to be higher among people affected by or interested in this condition. Indeed, of those survey respondents who said they had heard of nanomedicine being used in their condition area, just under 90 per cent (25 out of 29 respondents) gave Parkinson's Disease as their condition area. In comparison, over half of those who had not heard of nanomedicine being used in their condition area listed a range of conditions other than Parkinson's.

However, this does not explain the full picture because just over half of the total number of survey respondents affected by/interested in Parkinson's nonetheless said that they had not heard of nanomedicine being used in their condition area. In the focus group no-one had heard of nanotechnology or its use in their condition.

There were also geographic variations. For example, all Swiss respondents were affected by/interested in Parkinson's (thanks to the enthusiastic participation of a Swiss patient group), and a very high 20 out of 29 of these were aware of nanomedicine being used in their condition area. This compared to a much lower 4 out of 29 of the UK respondents affected by/interested in Parkinson's. There were mixed responses from countries with lower overall numbers of respondents, but due to the small numbers involved no conclusions can be drawn from this.

The research suggests that the actual use of nanomedicine in a particular condition area does not guarantee that patients will automatically be aware of this, although it might make it more likely. For conditions where the use of nanomedicine is further along the horizon, it is therefore unsurprising that levels of awareness are significantly lower. It also suggests that in most countries there may be considerable room for improvement in raising patients' awareness of nanomedicine.

ii. Raising Patients' Awareness of Nanomedicine

Another salient finding from the Patients' Needs Working Group's research - and arguably an unsurprising one given the preceding section - was that **80 per cent (68 out of 85 respondents) of survey respondents said they would like to receive more information about nanomedicine.** The percentage was even higher for some types of respondents: all patient organisation leaders who responded said that they would like to receive more information, as did almost 90 per cent of carers (7 out of 8).

Of those survey respondents who said that they would like more information on nanomedicine, **over 80 per cent (57 out of 68) said they would like to receive this information on the internet.** Over half of the patients and carers at the focus group agreed, as did all the patients and carers interviewed for the qualitative research, with almost 30 per cent wanting paper-based information. Internet, followed by paper-based information, were also the two top choices when responses were also analysed by type of respondent.

With regard to the sort of information that patients want, in the words of some of the interviewees, this should include:

- "factual information in lay terms" - there was consensus among interviewees that the information should be presented in a lay format to enable patients to make informed decisions on their treatment;
- "updates on where the research is currently at"; and
- "pros and cons".

Views on the desired sources of this information were mixed. Over 60 per cent (41 out of 68)³ of survey respondents who wanted to receive more information thought that it should come from clinicians. This is possibly because doctors are consistently viewed as trusted sources of information. Similarly, over half of the focus group attendees thought that the information should come from health care professionals (Specialist Nurses and GPs).

Just over half of survey respondents and interviewees said that information should come from patient organisations. This figure rose to three quarters of the focus group attendees, possibly due to the fact that all those present were already members of a patient organisation, whereas many of those who responded to the survey were not.

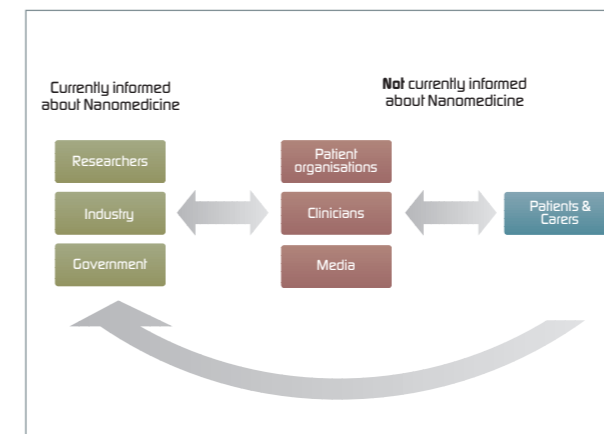
A third of people participating in the online survey and over half of attendees at the focus group wanted to see the media providing information on nanomedicine. Just over three quarters of those surveyed would not look to their national

government to provide information on nanomedicine, and only 9 out of 68 respondents said that they would look to the European Institutions. This means that other stakeholders need to work harder to ensure that they provide patients with this information.

This raises the question as to how to improve levels of awareness among patient organisations and clinicians, not least given the demands on their resources. Given their potential to reach the widest audience, the media also need to be provided with appropriate information to ensure balanced reporting.

It seems reasonable to suggest that those who are actually conducting nanomedicine research and/or developing nanomedicine products are best placed to inform those audiences from whom patients wish to receive information about nanomedicine. In turn, informed patients would be able to feed back into the research agenda, making this information process beneficial to all stakeholders concerned. This is illustrated by Figure 1 below.

Figure 1 – Suggested information flow to and from patients



With this in mind, the European Technology Platform (ETP) Nanomedicine seems to be ideally placed to contribute to improved information provision to patient organisations (and other key audiences). It is a current initiative led by industry and established together with the European Commission, and it brings together a wide range of large industry, SMEs, industrial associations, research institutions, academia and hospitals from across Europe. The ETP has identified dissemination of knowledge, ethical and safety concerns and "input from other stakeholders like insurance companies or patient organisations" as playing an important role in the priority topics on which it is focussing, so it should be involving them. The "NANO futures" European Technology Integration and Innovation Platform in Nanotechnology (ETIP) initiative currently being established should play a similar role.

Recommendation 1

The European Technology Platform on Nanomedicine and "NANO futures" European Technology Integration and Innovation Platform in Nanotechnology, together with the European Patients' Forum, should explore the involvement of patient organisations in the work of the Platforms, to provide input from patients' perspective and improve patients' understanding of nanomedicine. For these reasons, patient organisations' views should also actively be sought as part of any other nanomedicine strategy development at EU level.

However, to ensure that information on nanomedicine is communicated as widely as possible steps should be taken by a number of key stakeholders.

Recommendation 2

The European Commission has produced much useful information on the internet on nanotechnology aimed at the general public, e.g. short films, leaflets and brochures. It should organise the production of similar lay information on nanomedicine, which could be used by patient organisations, clinicians and the media.

National governments should also take steps to increase their dialogue with patient organisations on the development and use of nanomedicine. This is covered in more detail by Recommendation 7. In addition, industry and research associations have an important role to play.

Recommendation 3

European-level trade and research associations should produce lay information using stakeholder dialogue on nanomedicine research. National-level trade and research associations should disseminate this information in their country's language(s) to patient organisations, media and bodies representing clinicians. The European Commission should investigate what existing programmes should or could fund this, and/or develop new funding streams where required, e.g. science and society programmes or European Science Foundation.

However, to be as effective as possible, improving patient awareness of nanomedicine needs to be a two-way process. This is reliant on patient organisations also taking some responsibility for informing first themselves (e.g. with the assistance of their scientific/medical advisers) and subsequently both patients and their carers.

Recommendation 4

Patient organisations should be supported by the European Commission to investigate whether nanomedicine is currently or potentially useful in treating their condition, and if so to enable engagement in nanomedicine with a view to providing balanced information to patients and carers.

³ N.B. respondents were able to choose more than one option in the section of the survey on information provision, so overall responses may total more than 100 per cent.

¹ <http://www.etp-nanomedicine.eu/public/about/objectives-mission>

² Nanotechnology-based diagnostics including imaging; targeted drug delivery and release; and regenerative medicine.

Recommendation 5

The European Commission, working with the European Patients' Forum, should identify and engage with patient organisations that already communicate to their members on nanomedicine, and work with them to produce a 'best practice' case study and toolkit (e.g. FAQs, webpages, short files) to help guide and support other patient organisations.

Patient Support for Nanomedicine**i. Use of Nanotechnology in Medicine**

As part of the Patients' Needs Working Group's quantitative research, survey respondents were asked whether they supported the use of nanotechnology in medicine, on a scale of 1 to 5, with 1 being "not at all" and 5 being "strongly". Over 60 per cent, 53 out of 85 respondents, supported the use of nanotechnology in medicine "strongly" or "quite strongly" (5 and 4 respectively), with over 40 per cent of those who replied to this question supporting it "strongly". Fewer than 10 per cent selected 1 or 2.

Interestingly, prior awareness or knowledge of nanomedicine did not appear to make a significant difference to levels of support. In fact, of those survey respondents supporting nanomedicine "strongly", a higher proportion – over half – had not heard of nanomedicine being used in their condition area.

The interviews conducted as part of the Working Group's research suggest that the reason for this could be patients' willingness in some cases to accept higher levels of risk to find a cure or treatment. Indeed, the majority of interviewees thought that nanomedicine would be useful in the treatment of their condition. However, there was confusion as to how nanomedicine could be useful.

ii. Nanomedicine Research

The Patients' Needs Working Group's research indicates that the majority of patients view nanomedicine as a technology that could address many unmet medical needs and that patients want to see nanomedicine research taking place.

Support for nanomedicine research was also high. 53 out of 85 respondents to the survey question on research said that, within current spending, they would like to see more nanomedicine research into their condition. Among leaders of patient organisations and carers/relatives support for research support was also high: 8 out of 11 and 5 out of 8 respectively.

The qualitative research undertaken for this report suggests that support for nanomedicine research increases with the provision of information. Based on the information given to

them in a slide presentation, over 90 per cent of the 12 patients and carers interviewed said that research into nanomedicine should be continued, not only in their condition area but in all areas.

Recommendation 6

The European Commission and national governments in consultation with patient organisations should continue to discuss priorities for nanomedicine and fund their research and development. To ensure complementarity and avoid duplication, the European Commission should encourage the integration of national nanomedicine strategies.

Views on Safety and Risk**i. Safety and Risk**

Compared to other areas of questioning, views on the safety of nanomedicine were more mixed. On a scale of 1 to 5, with 1 being "not safe at all" and 5 being "very safe", 24 out of 85 (almost 30 per cent) of respondents chose 4, with 13 of the 85 respondents opting for 3. Notably, the highest proportion (26 respondents) selected "don't know".

One survey respondent specifically commented: "I believe that nanomedicine, like other technologies, has great potential probably both for good and for harm. Proper, but reasonable and balanced, controls will be needed to get the maximum benefit with the minimum harm."

Likewise, the qualitative research also elicited a wide range of responses on the issue of safety. Although many of the interviewees had concerns about the development of the research, based on the information presented to them they made a risk judgement and supported the technology with appropriate regulation.

Prior awareness of nanomedicine appeared to influence views on safety: it was notable that the interviewees who were concerned about the safety of nanomedicine did not have prior knowledge of nanomedicine. Similarly, of those surveyed who "didn't know" whether nanomedicine was safe, ten times as many had not previously been aware of nanomedicine being used in their condition area than had been aware of this.

It could therefore be concluded from the Patients' Needs Working Group's research that patients do not view nanomedicine as inherently unsafe. Nonetheless there is a lack of clear understanding about the potential safety aspects that may be unique to nanomedicine. This should be addressed not only through appropriate safeguards but also the communication of information. As one interviewee put it: "I would like for someone to get across what the advantages and disadvantages are to patient groups". This could be

addressed by Recommendations 1 to 4 as well as Recommendation 7, which would have the dual effect of improving patients' understanding of the risks and benefits, and also providing an official conduit for giving their views to government.

Recommendation 7

Where governments have organised stakeholder fora to discuss the potential risks and benefits of nanotechnologies including nanomedicine, they should encourage patient organisations to participate. Where such fora do not exist, governments should urgently consider establishing them.

ii. Other Observations

The Working Group's qualitative research indicated that there were mixed views among patients in terms of whether nanomedicine was regarded as different from any other new types of medical research. Just over half of the interviewees thought that nanomedicine was simply the next step in medical research, whereas others thought that it was "a new branch" of medical research and "completely different in terms of technology".

Due to patient groups' financial constraints, the Working Group was unable to focus in greater detail on ethical issues. However, this is an important area on which it would be helpful to gain further insight.

Recommendation 8

The European Commission should provide funding for focus groups and other participatory methods (e.g. citizen conferences, interviews, surveys) in a number of European countries, to identify and understand the spectrum of issues that nanomedicine raises for patients and their families.

ACCESS AND CLINICAL PREPAREDNESS**i. Access to Nanomedicine Products**

The timescale and funding of this project did not permit the Working Group to address issues surrounding access to nanomedicine products. However, given patients' evident support for nanomedicine and its potential to address unmet medical needs, this is an area that needs to be explored further, in order to establish:

- Whether current systems for Health Technology Assessment (HTA) and reimbursement processes can cope effectively with nanotech-derived products for diagnosis and therapy; and
- For patients, whether equity between diseases and across national boundaries can be achieved.

Recommendation 9

The European Commission should provide funding for a project examining access issues relating to nanomedicine products (diagnostic and therapeutic).

ii. Clinical Preparedness

A very small number of medical professionals responded to the Patients' Needs Working Group's online survey. Due to the small sample size and the fact that this was beyond the Working Group's remit, no conclusions have been reached on awareness of and support for nanomedicine among medical professionals.

However, having an informed clinical community is key, not least given the high importance that patients place on receiving information on nanomedicine from clinicians (see section above on 'Raising Patients' Awareness of Nanomedicine').

Recommendation 10

The European Commission should support further research to work with bodies representing clinicians and other healthcare professionals to: a) gauge awareness of novel possibilities arising from nanomedicine and incorporate these into clinical practice, and b) assist CPD/CME (Continuous Professional Development/Continuing Medical Education) to anticipate novel possibilities and formulate appropriate responses.

Concluding Comments

It is important to recognise that this report is very much a snapshot of a particular point in time. Patients' views on nanomedicine are likely to change as nanomedicine technology develops, so engagement with patient organisations needs to be undertaken on a sustained basis.

Crucially, however, nanomedicine is a novel area of medicine and as such it is a difficult area for patient organisations to explore. They have limited finances and are often run by volunteers or a small number of staff, so the opportunity for them to engage on issues such as this is constrained by resources rather than by willingness.

Consequently, if public bodies wish to engage with patient organisations on nanomedicine, as well as being sustained, consultation also needs to be realistically organised and funded.

Ethical and Societal Aspects of Nanomedicine

A Report by the NanoMed Round Table
Ethical and Societal Working Group

Summary and Recommendations

KEY POINTS

Ethical engagement with nanomedicine begins with the very concept of 'nanomedicine', a word that now groups diverse research activities together. Nanomedical researchers, physicians, patients and policy makers will all benefit when, on the basis of philosophical and social analysis, the programme and purpose of nanomedicine are better understood and more clearly defined.

The discussion of ethical and societal questions about nanomedicine must be informed by consideration of the feasibility of nanomedicine applications.

As well as the significance of nanomedical innovations, promises, hopes and anxieties should also be considered.

Low-income countries must be involved in the development of fair and sustainable global policy on benefit sharing in nanomedicine.



Approaching Nanomedicine: Ethical and Societal Issues

Questions which hitherto have become central to reflection on nanomedicine include:

- **The 'right not to know'** – The development of nanotechnologically-enabled diagnostic tools is likely dramatically to widen the gap between diagnostic capability and available therapies. What rights and means do citizens have not to know, or make known, the results of diagnostic tests?
- **The ethics of human enhancement** - How should we determine the permissibility and regulation of interventions that could be applied beyond the therapeutic contexts to enhance individuals' physical and mental capabilities?
- **Demographic effects** - The Nano Cancer Initiative of the US National Institutes of Health has claimed that, by 2015, no one will suffer or die from cancer. Although this seems unrealistic, such a drastic decrease of mortality would have a considerable impact on social security systems.

Such questions focus on applications (e.g. new diagnostic tools or brain-machine interfaces) which are envisioned by various promoters of nanomedicine and which resonate powerfully within popular culture. Their discussion relies upon the assumption that such applications are realistic in the short or medium term.

Recommendation 1

Since the discussion of implications of hypothetical but unlikely products is unhelpful, the European Commission and national governments should integrate the deliberation of ethical and societal issues with consideration of the feasibility of particular nanomedicine developments. This requires assessment of the visions driving nanotechnological developments, as well as historically and theoretically informed analyses of the cultural tendencies, societal aspirations, and commercial trends that influence nanotechnology for medicine and health.

Recommendation 2

The European Commission and national governments should support the development of a broader range of methodologies for research on the environmental, health and social (EHS) implications and the ethical, legal and social aspects (ELSA) of nanomedicine. This requires the explicit formulation of the criteria used to determine what is relevant for public deliberation.

Scientific and Technological Ambitions of Nanomedicine

Nanomedical research is hugely ambitious. In the search to understand and treat disease, it shifts attention beyond the cellular to the molecular level, and seeks to control a pathway from the molecular level right up to patients' and physicians' daily routines. Analysis of the scientific and technological ambitions of nanomedical research directs us to a view of nanomedicine as, primarily, basic research on the understanding, diagnosis and treatment of disease.

Moreover, the lack of a clear-cut definition of 'nanomedicine' could be an opportunity to configure nanomedical research so as to mark a departure from 'business as usual'. Some prominent actors in the field suggest that the novelty of nanomedicine is its adoption of a 'bottom-up' approach which draws on principles of self-organisation and on systems theory more generally. Accordingly, nanomedicine might be defined, for funding purposes, as medical research grounded in systems biology. The notion of the system encompasses many orders of magnitude, from the molecular level all the way up to societies and healthcare services, so this definition affords a unique opportunity to incorporate ethical and societal perspectives into the research process.

Recommendation 3

The European Commission's Research Directorate-General, the European Research Council and the European Science Foundation together with national funding agencies and research ministries, should initiate a deliberative process about the possibly distinctive features of nanomedicine that include its social and ethical dimensions. This process might include the development of roadmaps and should inform the setting of EU Framework Programme and national research agendas, and engage the scientific communities and their governing bodies, including academies of science.

Nanomedicine is the subject of high expectations and considerable public investment, but has yet to prove itself. In order to assess the value of basic nanomedical research, we might ask where a nanomedical approach is most productive and beneficial for researchers, healthcare systems and societies.

¹ This includes calls for research on foresight and technology assessment of nanomedical developments, as well as the design and evaluation of public engagement exercises.

Recommendation 4

Parliamentarians at EU and Member State level should conduct multi-stakeholder hearings that encompass public and world health advocates and patient groups. The aim should be to deliberate in a comparative manner the value of basic nanomedical research for prevention, diagnosis and therapy of disease. Scientific input should be provided from fields as diverse as medical anthropology, international law, bioethics and cancer research. Such hearings will focus and strengthen nanomedical research and raise public awareness of its possibilities and expectations.

Changing Conceptions of Medicine and Health

Health used to be defined as 'normal functioning', or as the absence of disease, but is now increasingly viewed as 'well-being', or as living to the fullness of one's capacities. Irrespective of whether and when nanomedical research lives up to its scientific and technological ambitions, it is already a part of these developments. A host of issues arises where commercial interests and medical research intersect. Nanotechnologically-enabled diagnostic tools, for example, expand possibilities of self-diagnosis and self-treatment, contributing to a reorganisation of medical expertise. At the same time, the marketing of diagnostic capabilities empowers individuals but also exploits their vulnerabilities and anxieties.

Recommendation 5

The European Commission and national governments should encourage social science and humanities research that goes beyond the risks and benefits of medical innovations to include the consideration of promises, hopes and anxieties. Such research should assess the emerging divisions of roles and responsibilities between patients, physicians, hospitals, e-health information systems, insurers and consumers. It should also identify safeguards that could and should be provided by public health care systems.

If health is defined as the absence of disease or as normal functioning, it is an unevenly distributed public good. However, when it is defined more broadly as living to the fullness of one's capacities, the gap between rich and poor countries widens further, broadening responsibilities and opportunities for benefit sharing.

Recommendation 6

The European Commission and national governments should create ways of involving low-income countries in the development of a fair and sustainable global policy on benefit sharing in nanomedicine. Avenues for this might include international organisations such as UNESCO and bodies which work towards and monitor the implementation of the United Nations Millennium Development Goals.

Approaching Nanomedicine: Ethical and Societal Issues

There have been many calls for an ethics of nanomedicine, and a number of authors and reports have discussed what this should look like or have surveyed the field as it currently stands. These should be understood as early attempts to come to terms with the emerging field of 'nanomedicine' (given that nanomedicine does not involve new forms of medical practice, a more appropriate label might be 'nanotechnological research for medicine and health'). As with all ethics for new and emerging science and technology (NEST-ethics), these first attempts at identifying ethical and societal issues follow familiar patterns. The Working Group therefore began its work by reflecting on the various ways in which nanomedicine has so far been approached.

For example, discussion of nanomedicine has often involved far-reaching visions promising entirely new ways of diagnosing, preventing, and treating disease. While it seems obvious that such new techniques will present new ethical and societal challenges, if the visions concern only the alleviation of human suffering it becomes difficult to see what these challenges might be. Accordingly, there is a tendency to simply call for further research on prospective technology assessment and potential ethical and societal issues. A response in the opposite direction imagines extreme ethical and societal problems which might appear if the most radical promises were fulfilled, such as the 'problem' of a world without disease, in which people live much longer and current social security systems would be overtaxed. Such speculation

requires excessive credulity about the likely success of nanomedicine, and has led to discussion of the pitfalls of 'speculative ethics' of nanotechnologies and nanomedical research.

One of the central questions in this debate is therefore whether ethical and societal issues should be discovered by imagining (and then discussing the ethics of) those diagnostic capabilities or therapeutic methods which are more or less likely. However, instead of trying to imagine possible outcomes and future applications, another approach might be to consider what we bring to nanomedicine.

The debate about speculative ethics shows that ethical and societal issues arising from nanomedicine cannot be considered in isolation from questions of what we know and don't know, or of how feasible different scenarios are. Accordingly, the Working Group recommends a process of integration of ethics and epistemology, sometimes referred to as vision assessment. This process requires more than the identification of particular technological trends, instead involving full consideration of how societies change alongside their technologies, and the development of detailed socio-technical scenarios. Debate about speculative ethics also shows that there are different ways of approaching the ethical and societal dimensions of nanomedicine. The Working Group encourages the development and pursuit of alternative methods to those which currently dominate debate.

Recommendation 1

Since the discussion of implications of hypothetical but unlikely products is unhelpful, the European Commission and national governments should integrate the deliberation of ethical and societal issues with consideration of the feasibility of particular nanomedicine developments. This requires assessment of the visions driving nanotechnological developments, as well as historically and theoretically informed analyses of the cultural tendencies, societal aspirations, and commercial trends that influence nanotechnology for medicine and health.

Recommendation 2

The European Commission and national governments should support the development of a broader range of methodologies for research on the environmental, health and social (EHS) implications and the ethical, legal and social aspects (ELSA) of nanomedicine. This requires the explicit formulation of the criteria used to determine what is relevant for public deliberation.

The Working Group identified a number of considerations which might be used to recommend or reject particular approaches:

- To what degree is the approach speculative, as opposed to grounded in sound judgements of feasibility?
- How concrete is the approach's orientation towards future applications, compared to its concrete focus on the priorities, values and expectations that currently motivate research and research funding?
- Is the main goal of the chosen method to achieve preparedness in the face of uncertainty about the future, or to empower citizens to deliberate current choices in research and development?
- Does the research seek to give expression to the concerns of stakeholders, publics, and citizens, or to develop findings which are historically and theoretically informed by bioethicists, historians of medicine, political theorists, sociologists and philosophers of science?

The Working Group followed its own advice on the importance of new approaches, choosing not merely to collate existing concerns around nanomedicine but rather to highlight areas of ethical questioning resulting from analysis of trends and expectations driving contemporary nanomedicine. The Group therefore sought to look beyond basic research, not so as to focus on potential futures, but rather by considering nanotechnologies for medicine and healthcare as the continuation of long-term developments within healthcare. **The ethical and social significance of nanomedicine lies in its invitation to question the place of medical research in medicine, healthcare, and society at large. In doing this it also challenges us to consider alternative ways of configuring science, technology and medicine so as best to support human flourishing.**

In adopting this approach the Working Group is suggesting an alternative to what is known as 'consequentialism'. Consequentialist ethics evaluates actions by considering their consequences or effects. According to consequentialism, technologies are judged by their outcomes or applications – if these are, for the most part, beneficial, then the technology is good. However, consequentialism is only one of a number of approaches to ethics, and a controversial one at that. Other approaches include 'virtue ethics', which emphasises the character of persons, institutions or traditions, and 'deontology', which is based on principles and rules about good actions.

Nanomedicine consolidates particular trends, expresses certain scientific ideas, pursues particular economic interests, and makes visionary promises: all of these carry values, norms, and ideas of the good life. These deserve ethical consideration, but are ignored within consequentialist approaches. In other words, whether good or ill comes from nanomedicine depends greatly on how the research enterprise is framed and conceptualised. The principles that lead us to dedicate public funds to nanomedical research and the character of European knowledge societies are therefore important features for any ethical analysis of nanomedicine.

The Working Group chose to take this comprehensive view, attempting to consider the forces shaping the development of nanomedicine. It placed the programmes and promises of nanomedicine in the context of long-term trends which have shaped – and will continue to shape – entire healthcare systems. It did this by drawing on academic expertise from disciplines including bioethics, human rights, philosophy of medicine, medical anthropology, philosophy of science and technology, history of medicine and public health.

Scientific and Technological Ambitions of Nanomedicine

Given the sheer breadth of research activities which the term 'nanomedicine' incorporates, the Working Group suggests that 'nanotechnology for medicine and health' is more appropriate. However, in doing so we may be giving up too soon: perhaps there is a way of using the term whereby nanomedicine appears as a new way of conducting research and of practicing medicine. Indeed, it might be a vehicle for achieving a new and better alignment of research and practice.

The Working Group proposes, then, that instead of merely observing what goes by the name of nanomedicine we take seriously the notion that **nanomedicine might be an opportunity to do things differently**. Discussion of nanomedicine can act as an invitation to researchers, physicians, patients, policy makers and publics to formally articulate their expectations of nanotechnology for medicine and health (e.g. as in the NIH Roadmap initiative in the USA).

² United Nations Educational, Scientific and Cultural Organization

³ www.un.org/millenniumgoals

⁴ E.g., European Group on Ethics 2007, Bruce 2006, Ach & Siep 2006, Ach & Lüttenberg 2008, Bawa & Johnson 2007, Ebbesen & Jensen 2006, Godman 2008, Gordijn^{2,2}

⁵ 2005, Grunwald 2005, Haker 2008, Horner 2005, Khushf 2007, Lenk & Biller-Andorno 2007, Weil 2003.

⁶ European Commission 2006, European Science Foundation 2005, Murday, J. S.; Siegel, R. W.; Stein, J.; Wright, J. F. 2009, NanoBio-Raise 2008. Swierstra & Rip 2007.

⁷ European Group on Ethics 2007, Sections 5.4.2 and 5.10.

⁸ National Science and Technology Council Report 1999, European Commission 2006, Max Planck Gesellschaft 2009.

⁹ DEEPEN 2009, Nordmann & Rip 2009, Roache 2008.

¹⁰ Brune, Ernst & Grunwald 2006, Grunwald 2005.

¹¹ Rip & te Kulve 2008.

Recommendation 3

The European Commission's Research Directorate-General, the European Research Council and the European Science Foundation together with national funding agencies and research ministries, should initiate a deliberative process about the possibly distinctive features of nanomedicine that include its social and ethical dimensions. This process might include the development of roadmaps and should inform the setting of EU Framework Programme and national research agendas, and engage the scientific communities and their governing bodies, including academies of science.

The Working Group arrived at such questions about the nature and purpose of nanomedicine on the basis of its analysis of nanomedical ambitions. At first glance, these resemble the ambitions of rational drug design, in which the development of new therapies is based on precise understandings of disease processes. In practice, these ambitions were never realised: the deliberate molecular construction of pharmaceutical agents proved less successful than traditional randomised search processes. Similarly, while genomics promised the discovery of the genes responsible for specific diseases it remains – several years after the conclusion of the Human Genome Project – questionable whether these ambitions will be fulfilled. Nanomedicine has also promised to provide new diagnostic tools and therapeutic interventions based on understanding and control of molecular processes in the cell. Will it suffer the same fate – that of exaggerated expectations – as rational drug design and genomics?

Based on such considerations the Working Group characterised nanomedicine in the following way: **Nanomedical research shifts attention beyond the cellular to the molecular level in the search for basic processes fundamental to the understanding and treatment of disease. It seeks to control a pathway which stretches from the molecular level all the way up to the daily routines of patients and physicians: it is thus a hugely ambitious project, and any scientific success may not, in the short or medium term, translate into significant innovations. On the other hand, it may be more productive than precursors such as rational drug design or genomics.**

If we understand the scientific and technological ambitions of nanomedicine in these terms, there are at least two alternative ways of framing it that deserve deliberation:

- i. Nanomedicine is part of a long tradition within the natural sciences towards analysis at deeper and deeper physiological levels. In this view, causes of and treatments for diseases should not be sought within environmental conditions, or even at the cellular level, but at the level of

molecular processes deep inside the cell. Taken to its extreme, this reduction of ordinary observable phenomena to fundamental physical processes amounts to the claim that "psychiatry is merely applied physics." Arguably, this could place nanomedicine on a path towards diminishing returns.

- ii. If we take seriously the (supposed) novelty of an emerging field of 'nanomedicine', this field might be viewed as a highly interdisciplinary science of complex systems. This science is based not only on an integrated physiological understanding of a tumour, for example, but is simultaneously based in stakeholder platforms answering to public interests. This new science might reorient the reductionist natural science tradition described in (i) above towards a multi-level approach to medical research. If health comprises not just physical but also mental and social well-being, then social and ethical considerations are not 'add-ons' to clinical nanomedicine but integral to it.

By deliberating these alternative pathways, patient groups, policy makers, scientists and health professionals can explore whether nanomedicine might create opportunities to integrate scientific understanding, medical practice, and ethical wisdom. Depending on the route taken, medical professionals could find themselves merely at the receiving end of technological development, or in a context in which medical experience and ethical considerations inform research in unprecedented ways, e.g. as outlined in the following four points:

- If the novelty of nanomedicine is defined only in terms of technical intervention at the nanoscale, nanomedicine is 'business as usual' simply taken to the next level of physiological understanding. Philosophical and social analysis has pointed out the pitfalls of this approach, e.g. the move from the cellular to the molecular level widens the already existing distance between medical research and practice. This ever-increasing distance poses problems for technological and economic development as well as unbridgeable discrepancies between the definition of a disease at the molecular level and the symptomatic experience of the disease in a therapeutic context.
- Associating nanomedicine with a novel way of thinking enables it to become a research enterprise dedicated, in an integrated manner, to the formation and re-formation of human well-being. The well-used notions of 'bottom-up engineering', 'systems and integrative biology', 'harnessing self-organisation', and 'complexity' suggest that central to this novel mode of thought is the behaviour and the dynamics of systems. If it were explicitly grounded in

systems biology, for example, nanomedicine would not be 'business as usual' because it would not be concerned merely with processes at the nanoscale but with interactions between different levels and scales as well. Its ambition would be to integrate observations at the nanoscale with those of humans in their environment. It could also seek to integrate the search for therapies with ethical and social conceptions of the good life.

- If nanomedicine is 'business as usual', the notion of 'personalised medicine' is misleading. By definition, a person is far more than a specific collection of genes but a social being with a unique biography. To offer 'personalised' treatment, then, requires more comprehensive understanding and appreciation than can be acquired by looking at genes, molecules and cells.
- Nanomedicine's scientific and technological ambitions suggest that it is not a short-term investment with immediate returns. A commitment to nanomedicine is a commitment to basic medical research, with the tenuous and long-term prospects of diagnostic and therapeutic benefits that this typically entails. Depending on which perspective one adopts, nanomedicine is either a long-term investment demonstrating the commitment of affluent societies to the best medical care for their citizens, or a misguided investment with little effect on sustaining healthy living globally.

Taken together, the considerations outlined above suggest that it is wrong to take nanomedicine as a given or to assume that it is only a matter of time until its benefits are forthcoming. Instead, the Working Group suggests that nanomedicine has yet to prove itself and should be evaluated in light of comparisons with other areas of health research, especially with regard to its overall contribution to prevention, diagnosis and therapy of disease and to the creation and preservation of conditions for healthy living.

Recommendation 4

Parliamentarians at EU and Member State level should conduct multi-stakeholder hearings that encompass public and world health advocates and patient groups. The aim should be to deliberate in a comparative manner the value of basic nanomedical research for prevention, diagnosis and therapy of disease. Scientific input should be provided from fields as diverse as medical anthropology, international law, bioethics and cancer research. Such hearings will focus and strengthen nanomedical research and raise public awareness of its possibilities and expectations.

Ethical engagement with nanomedicine therefore begins with the very concept of 'nanomedicine', a word that now groups together diverse research activities. Nanomedical researchers, physicians, patients and policy makers will all benefit when, on the basis of philosophical and social analysis, the programme and purpose of nanomedicine are better understood and more clearly defined.

Changing Conceptions of Medicine and Health

If medicine is the maintenance and restoration of health, then ethical, legal, and societal considerations of nanomedicine would at first glance appear to be confined to the narrow range of issues that arise in the process of moving people from an (undesirable) state of disease to a (desirable) state of health. However, health is no longer defined only as the absence of disease, but as well-being more generally. This broadening of scope opens the door to many challenges, such as the issue of human enhancement.

Nanomedical research is unlikely to introduce radically new techniques for human enhancement. The ethics of human enhancement are most fruitfully discussed not with regard to imagined nanomedical breakthroughs but by considering existing techniques such as sports drug-use or cosmetic surgery. These exist within a framework of ongoing trends, which are also taken forward by nanomedical research. Through an awareness of these trends, nanomedicine can be understood as incorporating broader notions of health as human wellness. Health used to be defined as 'normal functioning', or as the absence of disease; it is now increasingly viewed as 'well-being' or as living to the fullness of one's capacities. Irrespective of whether and when nanomedical research lives up to its scientific and technological ambitions, it is already a part of these developments. Areas such as e-health, point-of-care diagnostics, antibacterials, and neutraceuticals envisage nanotechnologies for medicine and health as part of a wellness market addressed to patient-consumers.

An analysis of nanomedicine in this context of changing conceptions of health and disease calls for consideration of the patient as consumer and in particular as a consumer of nanotechnologically-enabled diagnostic tools. These diagnostic tools have so far mostly been discussed in terms of 'the right not to know' and the increasing gap between diagnosis and therapy. This narrow focus needs to be widened, however, as so-called 'point-of-care diagnostics'

¹² NIH Roadmap for Medical Research 2006, Khushf 2008.

¹³ NanoBioRaise 2008.

¹⁴ Adam 2007.

¹⁵ An attitude encountered by one of the members of the Working Group.

¹⁶ Ahn, Tewari, Poon & Phillips 2006.

¹⁷ Ref. report by the Economic Impact Working Group.

¹⁸ Khushf 2007, Khushf 2008, Engel 1977.

¹⁹ Weckert 2008.

²¹ Müller 2009.

also provide scope for more expansive self-monitoring by healthy people and broaden possibilities of self-diagnosis and treatment which are already changing the definition of medical expertise. In the context of 'e-health', for example, the science- and technology-driven move towards point-of-care diagnostics and the commercial exploitation of anxieties are coming together in new divisions of labour in healthcare systems. These developments require careful monitoring and analysis, in particular the assessment of established and emerging divisions of labour amongst patients, physicians, hospitals and insurers. What are the implicit values driving these divisions of labour, and what should be done to ensure good practice?

Recommendation 5

The European Commission and national governments should encourage social science and humanities research that goes beyond the risks and benefits of medical innovations to include the consideration of promises, hopes and anxieties. Such research should assess the emerging divisions of roles and responsibilities between patients, physicians, hospitals, e-health information systems, insurers and consumers. It should also identify safeguards that could and should be provided by public health care systems.

Once health is broadly defined as well-being, the responsibility of benefit sharing with low-income countries is also broadened, creating opportunities for new modes of global interaction. The responsibility of benefit sharing is currently framed as compensation, i.e. medical research and development need to make up for past injustices, for example. If we understand health as well-being, however, macro-ethical considerations lead to wider, human rights-based notions of benefit-sharing. These ultimately aim at the restoration of human flourishing (as measured by improvements in quality of life or public health infrastructure). Such debates raise the question of how to define the responsibility of states or transnational entities towards low-income countries.

Recommendation 6

The European Commission and national governments should create ways of involving low-income countries in the development of a fair and sustainable global policy on benefit sharing in nanomedicine. Avenues for this might include international organisations such as UNESCO and bodies which work towards and monitor the implementation of the United Nations Millennium Development Goals.

²² Hastings Center Report 1996.

²³ European Group on Ethics 2007, section 5.6.

²⁴ E.g., European Commission 2006, p. 24.

²⁵ Boenink 2009.

Concluding Comments: Further Issues for Consideration

The Working Group had much more to say than has been possible to include in this report, having discussed issues such as:

- the 'metaphysical research programme' of nanomedical research, its implicit assumptions about the human body, health and illness, and technology and nature, and how these might challenge more traditional conceptions;
- regenerative medicine and tissue engineering, the integrity of the patient's body and the changing character of medicine as it moves from the art of healing to the engineering of replaceable body parts; and
- the development of new analytic tools which can quickly obtain overwhelming amounts of data from a drop of blood. How might this 'data overload' alter the concept of 'meaningful information' for patients and doctors? What is the value of information? Are there issues of confidentiality and privacy related to such techniques?

By highlighting the recommendations in this report, the Working Group has signalled that ethical and societal deliberation confronts a far wider range of issues than those of safety and risk that are generally recognised. At the same time it has emphasised an approach in which ethics goes beyond questions of risk not by looking into the distant future, but by asking how nanomedical research intensifies current trends and engages with choices that are before us today.

For a desperately ill patient, hope is a real achievement. Societies also hope for a better future, and often pin these hopes on emerging technologies. Ethical and social analysis of emerging technologies, however, should be careful not to take as fact what at this point is only a matter of hope. Such analysis must take hopes and concerns about the future seriously, but do so without second-guessing what the future will hold. We should ask of nanomedicine what trends it continues, problems it intensifies, and promises it holds out. In this way we can evaluate what measure of public support these promises deserve.

²⁶ Presentation by Susana Vidal at Working Group meeting.



Economic Impact and Understanding of Nanomedicine

A Report by the NanoMed Round Table
Economic Impact Working Group

Summary and Recommendations

KEY POINTS

Reliable data is needed to predict the impact of nanomedicine on healthcare costs and benefits, and market growth.

If urgent action is not taken, the current lack of data and economic models will hinder the development of nanomedicine in Europe.

Early health economics assessment is crucial to recognise the potential applications of nanomedical innovations as early as possible and therefore enable maximum patient benefit.

The future impact of nanotechnology innovations in healthcare systems, and their added value in preventive medicine, should be assessed.

Action is required to ensure the effective organisation of nanomedicine in Europe and Europe's competitiveness in the face of worldwide competition.



The Importance of Assessing the Economic Impact of Nanomedicine

The potential of nanomedicine to diagnose, treat and prevent diseases has been recognised, but its cost-effectiveness is not well developed in the public framework. Since each Member State applies different reimbursement rules, the lack of data and economic models will hamper the development of nanomedicine in Europe.

How Should the Economic Impact of Nanomedicine be Evaluated?

Nanotechnology will be considered in health economics only if it brings significant added therapeutic value. Data on clinical effectiveness must therefore be acquired prior to any attempt to evaluate economic significance. Societal and economic criteria (going far beyond the cost of treatment) also need to be taken into account.

Measuring and Maximising the Positive Economic Impact of Nanomedicine

Addressing the Current Lack of data

Up to now health economics studies do not cover innovations coming from nanotechnology, so data regarding the economic assessment of nanotechnological innovations in the healthcare sector is scarce.

Recommendation 1

Companies and clinicians should produce data based on well-defined criteria of cost-effectiveness for the economic evaluation of nanotechnology-based innovations in clinical trials and health technology assessment studies.

Early Health Economics Assessment

Early medico-economic assessment is critical to recognise as early as possible (ideally at the pre-clinical stage) the potential applications of nanomedical innovations; this enables assessment of maximised therapeutic value for patients.

Recommendation 2

The European Commission and national governments should promote and support projects in partnership with health economists, technology developers, clinical researchers, healthcare providers and patient associations, with comparisons across Europe, to assess the cost effectiveness of nanomedical innovations as early as possible.

Reimbursement Issues

When added therapeutic value is clearly demonstrated, e.g. in the case of unmet medical need, reimbursement generally occurs. However, nanotechnology is most often considered as one innovation among others, without recognising its deep impact on the definition of medical practices.

Recommendation 3

National reimbursement agencies, along with public and private insurers, should establish a European working group to consider the future impact of innovative approaches in healthcare systems across Europe, taking nanotechnology as a case study.

Preventive Medicine and Monitoring of Chronic Disease

Nanotechnology applications may offer new solutions for preventive medicine and the growing need for diagnostic and monitoring tools. The added value of nanotechnology for consumer-driven markets in healthcare and well-being must also be considered.

Recommendation 4

The European Commission should launch a health-economics project to assess the economic impact and emergence of new cost models relating to nanotechnological innovations in preventive medicine and the monitoring of chronic diseases.

Effective Organisation of Nanomedicine in Europe

This is critical to avoid false investments, optimise clinical benefits and therefore to maximise economic impact.

Recommendation 5

The European Commission and national governments (especially health and research ministries and bodies) should establish technology-specific reference centres linking early development with clinical research and clinical practice. These centres should be partially publicly-funded.

Worldwide Competition in Nanomedicine

Europe's competitiveness must be ensured at every level of nanomedicine investment, from basic research to reimbursement.

Recommendation 6

The European Commission should share the conclusions of the NanoMed Roundtable with international expert groups in order to improve European and international strategies for maximising the positive economic impact of nanomedicine.

The Importance of Assessing the Economic Impact of Nanomedicine

In addition to its main applications in diagnosis, drug delivery and various therapeutic effects, nanotechnology is also our best hope for regenerative medicine, with significant achievements realised in recent years in the laboratory. Nanotechnology is also of great interest for cancer diagnosis and treatment, both in preventive and curative approaches.

This has been recognised in Europe with the EU project Nano2Life (Network of Excellence), which has established detailed objectives for nanobiotechnology development, starting with clinical needs in the field of neurosciences and oncology.

However, the cost-effectiveness of nanomedicine (for all fields of application, including drug development) is not well developed within the public framework. This could hamper the development of nanomedicine in general, and in Europe in particular.

Since each EU Member State applies different rules for reimbursement, the lack of data and economic models constitutes a weakness that will hinder or even block the development of innovative procedures.

In the short-term this would particularly affect cancer diagnostics and treatments. Longer term, the absence of economic models and aggregated data regarding the cost-

¹ Annex 1 provides some snapshots about the most promising aspects of nanotechnology in medicine.

² The main conclusions of the Working Group's data collection is provided in Annex 1, and key references are outlined in Annex 2.

³ VDI, Bionest, Business Insights, Visiongain.

⁴ US Food and Drug Administration (FDA) and some national databases.

⁵ www.clinicaltrials.gov

⁶ A liposome is a tiny bubble made out of the same material as a cell membrane. Liposomes can be filled with drugs, and used to deliver drugs for cancer and other diseases. (<http://en.wikipedia.org/wiki/Liposomal>)

⁷ Bionest 2008

⁸ Visiongain 2006

⁹ Frost and Sullivan 2007

¹⁰ Lux Research 2009

¹¹ Bionest 2008

effectiveness of nanomedicine could endanger the potential of nanotechnology to prevent/treat other diseases (including rare genetic diseases, neurodegenerative diseases and chronic diseases, for example), as well as the promising approaches provided by nanobioengineering in regenerative medicine.

The Current Landscape

- **Commercialised products** - Except for certain surveys, it is almost impossible to retrieve nanomedicines and medical devices integrating nano features from existing approved drugs and devices databases. The “nano” feature is simply not indicated. However, the Working Group counted about 45 products commercialised in 2008 (developed mainly by US companies), of which only two products were diagnostics.
- **Pipeline and products under development** - Information about product pipelines and products under development is scarce and not comprehensive. Consultants often refer to companies active in nanotechnology, developing various applications including healthcare products. Communication is therefore targeted towards investors. There is no public information about products under development by large companies in the healthcare sector, e.g. pharmaceutical, diagnostics or medical devices companies.

The Working Group’s preliminary research identified about 60 products under development, although this figure is an estimate, since the group did not have access to primary sources (companies). A preliminary search of the US National Institutes of Health’s clinical trials database revealed 69 results containing the word “nanoparticle” and 372 results containing the words “liposome or liposomal”.

- **Market surveys** - Absolute values of markets are very difficult to forecast. A detailed analysis of pipelines and reimbursement issues would be required to do so, but this is never addressed by market surveys. However, the Working Group purchased excerpts of three surveys that have been evaluated as more reliable than others. The most recent of these estimated the value of the final (global) market of nanomedicine drug delivery products at US\$ 4,181 million in 2007. Estimations of the value of nanomedicine’s future markets are US\$ 19,262 million in 2011 and US\$ 27,700 million in 2014.

The most interesting strategic analysis considers that products are enabled by nanotechnology, whatever the application. Therefore the market of nanotechnology for healthcare comprises nanomaterials, nanointermediates and final products (integrating nano features). Nanomedicine is definitely not a market segment.

- **Companies** - The Working Group identified a preliminary list of companies involved in nanomedicine products: 19 in Germany, 12 in France and 9 in the UK.

How Should the Economic Impact of Nanomedicine be Evaluated?

i. Clinical Effectiveness

Nanotechnology will be considered in health economics only if it brings a significant added therapeutic value, which depends on each particular situation (from unmet medical need to incremental improvement of patient care). Therefore, it is of primary importance to acquire data on the clinical effectiveness of nanotechnology, prior to any attempt to evaluate economic relevance.

ii. Societal and Economic Criteria

The economic impact of nanomedicine has to be considered in a general model that integrates relevant criteria going far beyond the cost of treatment itself, and asks the following three questions:

1. To what extent does nanotechnology contribute to new health products and services, and what is the future wealth generated?
2. How much does nanotechnology contribute to a change of cost models of the health systems?
3. How much are the two previous questions influenced by the regulatory framework, which basically is a result of social and political pressure?

An ideal model to assess the economic impact of nanomedicine would integrate parameters relating to societal and economic criteria:

- **Wealth created by nanomedical innovations**
 - Industrial property value (patents and licences).
 - Markets and turnover for companies, due to new products and services.
 - Existing jobs and new jobs in companies and services.
- **Costs relating to regulation for all stakeholders** (e.g. regulatory agencies, reimbursement agencies, companies, technology developers)
 - Additional costs relating to the establishment of new procedures (e.g. combination products), evaluation of materials, and relevance of manufacturing standards.

¹² This results from the Economic Impact Working Group’s discussions rather than academic review.

¹³ Ref. Regulation Working Group of the NanoMed Round Table.

- **Economic costs and benefits in the healthcare system**
 - Public and private “out of pocket” expenditures for the new treatment.
 - Cost-benefit-ratio of standard treatment compared to the nanomedicine treatment.
 - Patients’ access to innovative (often expensive) diagnostic procedures and treatments through national reimbursement systems.
 - Costs relating to breakthrough innovation (if innovation creates new costs).
 - Costs relating to assessing so far potential/unknown long-term effects.
 - Economic benefits induced by health innovation (e.g. efficacy, fewer side effects, reduction of length of hospital stay, added month/years of life, added quality of life) and transformation of social benefits into economic benefits.
- The power of public perception
- Towards nanotechnology, including other applications such as cosmetics, food, consumer products.
- In terms of health expectations, e.g. policies, access, costs.

Analysing the economic impact of nanomedicine is therefore complex. Nanotechnology produces incremental innovation in medicine but also more radical changes in diagnostics and therapeutics, pushing away the boundaries between curative and pre-emptive medicine.

Evaluating the economic impact of such medical innovations cannot be done without a clear analysis of healthcare cycles. For example, an increased cost in early diagnostics can be very effective later in terms of benefits.

Measuring and Maximising the Positive Economic Impact of Nanomedicine

i. Addressing the Current Lack of Data

Health economics is a complex area. There are different healthcare systems in Europe, with different criteria (e.g. Quality Adjusted Life Years in the UK and cost/benefit in Germany and France) with various reimbursement tracks and procedures. Data aggregation is therefore difficult.

Health economics studies currently do not consider innovation coming from nanotechnology, so data regarding the economic assessment of nanotechnological innovations in the healthcare sector is scarce.

The Working Group conducted a systematic search on public Health Technology Assessment databases but did not find any survey or evaluation regarding nanomedicine, nanotechnology or nanoparticles. The Working Group did find

¹⁴ www.ifeg.de

¹⁵ Patients with an abnormally low number of white blood cells

three examples of economic assessment related to liposomal doxorubicin (for ovarian cancer) and amphotericin B (an antifungal prophylaxis for neutropenic patients). These products have been used for many years in clinical practice, but in the case of amphotericin B the Working Group found two surveys (both based on efficacy/cost analysis and for the same medical objectives) that reached opposite conclusions as to whether it was economically worth providing the product. This shows that the criteria that are needed for evaluation can vary significantly (e.g. what is a severe side effect?) and that this does not make economic evaluation an easy task.

Health economists need data from clinical research and practical application in order to conduct an economic evaluation of any nanomedical innovation.

Recommendation 1

Companies and clinicians should produce data based on well-defined criteria of cost-effectiveness for the economic evaluation of nanotechnology-based innovations in clinical trials and health technology assessment studies.

ii. Early Health Economics Assessment for Nanomedicine

The Working Group concluded that: “It’s always too early to assess until suddenly it’s too late”.

Nanotechnology researchers may not have the right understanding of the added therapeutic value of their innovation. Without blocking developments, it is important to recognise as early as possible (ideally at the pre-clinical stage) the potential applications of a given nanomedical innovation. This early recognition of applications would enable assessment of maximised therapeutic value for patients, which could take the form of efficacy, effectiveness, outpatient rather than inpatient treatment, shorter hospital stays, fewer drugs, patients’ acceptance of, and compliance with, the treatment. In turn, this will define the future access to markets, and therefore market volumes.

Commercial market surveys most often consider nanomedicine market volumes without any reference to its real therapeutic added value. Even when the assumption is addressed (e.g. one market analysis considered by the Working Group considers that nanotechnology, as an “enabling” technology, will progressively penetrate existing markets), it is never based on a precise market segmentation, which is fundamental to provide reliable market studies.

Recommendation 2

The European Commission and national governments should promote and support projects in partnership with health economists, technology developers, clinical

¹⁶ Lux Research 2009

researchers, healthcare providers and patient associations, with comparisons across Europe, to assess the cost effectiveness of nanomedical innovations as early as possible.

The implementation of Recommendation 2 could lead to a continuous health-economic assessment of nanotechnology in medicine, for instance in the shape of specific projects, a permanent working group, or an exchange platform connected to the European Technology Platform (ETP) on Nanomedicine or "NANO futures" European Technology Integration and Innovation Platform in Nanotechnology. This early medico-economic assessment is critical to make market projections more reliable.

iii. Reimbursement Issues

Several national agencies responsible for guidelines leading to reimbursement decisions were invited to take part in the Working Group's discussions but were unfortunately unable to join us (e.g. Haute Autorité de Santé – HAS (France), National Institute for Health and Clinical Excellence – NICE (UK), Institute for Quality and Efficiency in Health Care – IQWiG (Germany)). Therefore our recommendations do not take into account the position of these stakeholders, who might have a different idea of nanomedical innovations.

When added therapeutic value is clearly demonstrated, e.g. in the case of an unmet medical need, reimbursement generally occurs. When a balance between the cost of treatment and induced benefits (e.g. quality of life, short/long term side effects, hospital costs) needs to be established, each country manages its economic compromises following specific guidelines.

However, nanotechnology is most often considered as one innovation among others, without really recognising its deep impact on the definition of medical practices.

Recommendation 3

National reimbursement agencies, along with public and private insurers, should establish a European working group to consider the future impact of innovative approaches in healthcare systems across Europe, taking nanotechnology as a case study.

The objective of this working group could be to analyse in detail, in a forward-looking approach, the social and economic consequences of nanomedical innovations and their implications for health policies in the Member States.

iv. Preventive Medicine and Monitoring of Chronic Disease

Nanotechnology is most often considered as being of great interest for early diagnostics and targeted therapies, in the

current scheme of curative medicine. In addition, **nanotechnology applications may offer new solutions for preventive medicine and the growing need for diagnostic and monitoring tools, especially for patients with chronic diseases but also for healthy people.** Nanotechnology can also bring innovation in miniaturisation and functional complexity for point of care or wearable devices.

Consequently, new business models will begin to emerge. Many Framework Programme 7 (FP7) projects address this challenge, but **the added value of nanotechnology for more consumer-driven markets in healthcare and well-being must also be considered.**

Recommendation 4

The European Commission should launch a health-economics project to assess the economic impact and emergence of new cost models relating to nanotechnological innovations in preventive medicine and the monitoring of chronic diseases.

v. Effective Organisation of Nanomedicine in Europe

A good organisation of nanomedicine in Europe is of critical importance to avoid false investments, optimise clinical benefits and therefore to maximise economic impact. The ideal configuration of centres of reference (or networks) could be as follows:

- Basic research and early technology development in public or private research institutes (as in the Nanomedicine Centers of Excellence in the USA).
- 'Technosensitive' clinical researchers (i.e. researchers who are interested in and can understand technology, especially nanotechnology) recruited in clinical networks (e.g. the European Organisation for the Research and Treatment of Cancer) to develop clinical research about nanomedicine, working closely with nanotechnology researchers and pharmaceutical/medical technology companies.
- Support from experts in health economics assessment, dealing with specific studies in selected areas.
- All stakeholders in the three previous points taking part in a thorough safety assessment (covering, for example, toxicity, side effects, ecotoxicity and long term effects) in order to balance possible benefits.
- Patient associations participating as leading observers and advisers from the inception of technology developments.
- Representatives of the fields of ethics, regulation and communication need also to be involved from the outset.

Recommendation 5

The European Commission and national governments (especially health and research ministries and bodies) should establish technology-specific reference centres linking early development with clinical research and clinical practice. These centres should be partially publicly-funded.

In order to facilitate Recommendation 5, the results of the NanoMed Round Table should be disseminated to existing networks and projects related to nanomedicine, including:

- Nanomedicine ETP (European Technology Platform)
- CLINAM (European Foundation for Clinical Nanomedicine)
- ERANET nanomedicine
- Euronanobio FP7 project
- EORTC (European Organisation for the Research and Treatment of Cancer)
- EMIL (European Network on Molecular Imaging)
- Conticanet FP6 network (Connective Tissue Cancer Network)
- European JTI IMI (Joint Technology Initiative in medicines: Innovative Medicines Initiative)

vi. Worldwide Competition in Nanomedicine

In parallel with the recommendations outlined above, **it is equally important to take account of the international context of nanomedicine investment in order to ensure Europe's competitiveness in the face of worldwide competition. This applies to every level of nanomedicine investment:** basic research, clinical research, economic, social and ethical evaluation and reimbursement.

It is clear that the importance of nanomedicine has been recognised internationally. For example, in the USA the National Institute of Cancer has established an Alliance for Nanotechnology in Cancer, which drives many research projects to maximise benefits for patients.

Due to the financial and time limitations of this project, the Working Group was unable to focus in detail on the international context. However, this is an important area and there are key issues on which it would be helpful to gain further insight, such as the consequences of the current evolution of the American healthcare system, and whether the strategies of leading US companies in Europe will change.

Recommendation 6

The European Commission should share the conclusions of the NanoMed Roundtable with international expert groups in order to improve European and international strategies for maximising the positive economic impact of nanomedicine.



Establishing a Science-based Societal Learning Mechanism and Understanding of Nanomedicine

A Report by the NanoMed Round Table
Regulatory Working Group

Summary and Recommendations

KEY POINTS

In order to enable responsible innovation in nanomedicine, the regulatory framework should facilitate a scientifically-based societal learning process, i.e. by being flexible enough to allow society to acquire, exchange and accumulate knowledge and experience in dealing with a new technology.

For effective implementation of the existing regulatory framework, there is a need for better coordination and harmonisation of regulatory procedures, especially those on reporting and data collection.



Boosting the Effectiveness of Existing Regulation

Better coordination and harmonisation of existing regulatory procedures is urgently needed to facilitate data collection and improve regulatory clarity. Priorities are the clarifying of the regulatory pathway for 'combination products' (which bear the features of different medical products and even food or cosmetic products), defining common terminology and relevant data, and promoting data collection efficiency.

Recommendation 1

At the current development stage, regulatory policy should focus on promoting the harmonisation and responsiveness of existing regulatory systems. The European Commission should establish and promote supporting mechanisms that boost the effectiveness and responsiveness of the existing regulatory framework.

Recommendation 2

The European Commission should strengthen its efforts to clarify the regulatory pathway and classification of combination products in the EU, and actively seek international collaboration to improve consistency between different jurisdictions.

Recommendation 3

The European Commission should strengthen its efforts to clarify the regulatory pathway and classification of combination products in the EU, and actively seek international collaboration to improve consistency between different jurisdictions.

Recommendation 4

The European Commission should take advantage of the merits of recent medical product regulation initiatives (e.g. seek international collaboration in establishing common reporting schemes to promote the efficiency and effectiveness of product authorisation), and use the Cross-border Healthcare Directive to facilitate data collection on common clinical issues and boost expertise for the clinical application of nanomedicine.

Ensuring the Responsiveness of Regulatory Policies

This requires, among other measures, meaningful engagement with users and stakeholders.

Recommendation 5

The European Commission should establish and promote early dialogue with the different stakeholders on regulatory issues concerning nanomedicine, and ensure the regulatory framework for nanomedicine is grounded in users' experience.

Recommendation 6

Patients' involvement in the nanomedicine policy making process should be institutionalised at both EU and national levels.

Recommendation 7

The European Commission should facilitate the accessibility of regulatory expertise by establishing user-friendly mechanisms which encourage early dialogue with regulatory bodies and regulatory partnership in order to facilitate consensus on data requirements.

Recommendation 8

The European Commission should:

- consider the appropriate application of the subsidiarity principle in regulating nanomedicine, taking into consideration national regulatory infrastructures and cultures. The need for capacity building at national level should also be addressed in EU regulatory policy.
- ensure regulatory policies take into account factors such as the situation in different Member States, different sizes of companies and different types and applications of nanotechnologies.

Recommendation 9

The European Commission should ensure continued efforts to address and monitor the health and environmental impact of nanomedicine, including improving awareness of environmental, health and safety (EHS) issues of nanomaterials, both in hospitals and nanomedicine companies.

Establishing Mechanisms of Credibility for Responsible Innovation

Mechanisms that offer credibility and authority are needed to support and encourage responsible practice in the development of innovative products.

Recommendation 10

The European Commission should support institutional mechanisms that facilitate a common perspective with regard to clarity, objectivity, and common practice for credibility and authority, e.g. joint efforts on development of testing protocols, standards and best practice.

The Economic Implications of Regulation

The cost of accessing regulatory expertise and meeting regulatory requirements can present significant barriers to bringing innovative nanomedicine to market.

Recommendation 11

Regulators should take into consideration the economic implications of regulation for nanomedicine, including impact on timeline, insurability and the funding support needed for access to regulatory expertise and extra compliance investment, especially for SMEs and academic institutions.

Enabling Responsible Innovation: Establishing a Scientifically-Based Societal Learning Process

The behaviour and functionality of many chemicals at nanoscale may differ substantially from their behaviour in bulk. This offers new opportunities and a wider diversity of applications, but may also raise new risks and challenges. An ongoing question is whether existing regulations are adequate for managing the new risks, while not unduly constraining research and innovation.

A prefix such as "nano-" does not necessarily imply novelty in scientific research or technological application. Even where there may be novelty, this does not imply either an automatic need for regulation, or an absence of coverage by existing regulation. The breadth of applications of nanotechnologies implies that some or all of these will be in fields that are already significantly regulated at national and European levels, as illustrated by the existing literature. However, with the current limitation of scientific knowledge, a regulatory framework that aims to enable responsible innovation is

needed, rather than a traditional reactive regulatory approach. This will facilitate scientifically-based societal learning, by being flexible enough to allow society as a whole the chance to acquire, exchange and accumulate knowledge and experience in dealing with a new technology.

The Regulation Working Group considers that no specific need for new legislation can be identified at the present time. However, several implementation issues have been identified as primary regulatory concerns. **Mechanisms to boost the effectiveness and responsiveness of the existing regulatory framework and to establish credibility for responsible innovation are of greatest importance** and are therefore the focus of this report.

Boosting the Effectiveness of Existing Regulation

Better coordination and harmonisation of existing regulatory procedures is urgently needed in order to facilitate data collection and improve regulatory clarity. This is crucial for advancing knowledge on safety, reducing disproportionate regulatory burden and improving the accessibility of new medicinal products.

Recommendation 1

At the current development stage, regulatory policy should focus on promoting the harmonisation and responsiveness of existing regulatory systems. The European Commission should establish and promote supporting mechanisms that boost the effectiveness and responsiveness of the existing regulatory framework.

Three immediate and priority targets for coordination and harmonisation are outlined in further detail below. These are:

- clarifying the regulatory pathway;
- defining common terminology and relevant data; and
- promoting data collection efficiency.

i. Clarifying the Regulatory Pathway

Nanomedicine provides great opportunities to integrate medicine, medical devices and other medical products (e.g. drug/device, device/implant). Many of the products will be 'combination products' or 'borderline products' that bear the features of different medical products and even products of adjacent areas such as food and cosmetics.

However, regulations on healthcare have generally been sector-specific. A recurrent problem in regulation is,

therefore, the overlap (or gap) between the regulatory systems and frameworks for different sectors. For example, EU legislation differentiates clearly between medicinal products and medical devices. For medicinal products there is a highly centralised system governing legal access to market, whereas medical devices are regulated under New Approach Directives, a more decentralised system.

In both systems, risk management is a key requirement guarding the quality and safety of products on the market. However, the regulatory approaches for risk assessment in these two fields differ (see Annex 1 for more information). Since new medicinal products – including those enabled by nanotechnologies – are increasingly resulting from converging technologies, levels of regulatory oversight on these products depend to a large extent on regulatory policy on 'combination' and 'borderline' products.

There is also inconsistency in new regulations on nanotechnology-enabled products in the adjacent areas of cosmetics and novel food. Food has been the subject of much regulatory debate, now including the regulation of food additives. The area of cosmetics is also carefully regulated, but is the subject of quite intense research and innovation which may raise new problems relating to consumer health.

Clarity in product classification is of primary importance for ensuring adequate regulatory oversight and estimating development cost. However, there is yet no shared understanding of what a 'combination product' is and how it should be regulated. It is not yet clear whether nanoscale products, or products that contain nanoscale materials, raise any novel questions relevant to their classification as biological products, devices, drugs, or combination products.

It is therefore not clear whether the current regulatory approach concerning combination products is able to address appropriately the regulatory needs of nanomedical products. Along with the inconsistency in new regulations on nanotechnology-enabled products in the adjacent areas of cosmetics and novel food, this means that **collaboration between the regulatory bodies at both European and international levels is crucial in improving consistency and clarity in regulation.**

Recommendation 2

The European Commission should strengthen its efforts to clarify the regulatory pathway and classification of combination products in the EU, and actively seek international collaboration to improve consistency between different jurisdictions.

ii. Defining Common Terminology and Relevant Data

Nanotechnology governance presents two types of regulatory issues:

1. generic issues originating from the special features of nanotechnologies; and
2. issues concerning general deficiencies of current regulatory systems that cause problems for all applicable products including nanomedical products.

In the second of the two points above, it is more appropriate to address the issues as general issues concerning all the applicable products instead of seeing them as nanotechnology issues. This report focuses on the question "What is 'new' about nanomedicine?" and therefore generic regulatory issues of nanomedicine. In order to identify such issues, there is an urgent need to establish common grounds for enabling comparable testing results, e.g. agreed common terminology and testing endpoints. Several international organisations have devoted significant efforts to this (see Annexes 5 and 6 for more details).

A primary question concerning medicinal products is how to generate the 'evidence' required to fulfil the safety and efficacy requirements in existing regulatory frameworks. Current regulation for medicinal products is well known for its stringency and long history of using risk/benefit comparison as evaluation tools. However, **when it comes to innovative nanotechnology products, it is not clear what methods and data should be considered appropriate and satisfactory for fulfilling the legal requirements of safety and efficacy.**

There is, therefore, an urgent need to improve the shared understanding on the nature of the data that are needed to establish safety and efficacy. The data requirements concerning clinical endpoints for evaluation of effect of the products are crucially important in ensuring safety and benefits for patients, as well as regulatory clarity for companies and the insurance industry.

Recommendation 3

The European Commission should devote efforts to defining common terminology and relevant data in nanomedicine, actively supporting the clarification of data requirements concerning safety, efficacy and clinical endpoints for the evaluation of effect of the products.

iii. Promoting Data Collection Efficiency

To promote the efficiency of data collection and reduce unnecessary duplication of reporting procedures, regulatory bodies should take advantage of the merits of several of the

latest initiatives in medical product regulation. These include the common reporting schemes established through the agreement between the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) on orphan drug authorisation, as well as the cross-border data collection procedure established in the Cross-border Healthcare Directive.

The EU has the advantage of data-generating capacity from all its Member States. Expert members of the NanoMed Round Table identified the cross-border data collection on common clinical issues as an important competitive advantage for the EU. The forthcoming Cross-border Healthcare Directive will create opportunities in data sharing through the establishment of 'centres of reference' that will create critical mass for research and boost expertise for the clinical application of new medical products.

Recommendation 4

The European Commission should take advantage of the merits of recent medical product regulation initiatives (e.g. seek international collaboration in establishing common reporting schemes to promote the efficiency and effectiveness of product authorisation), and use the Cross-border Healthcare Directive to facilitate data collection on common clinical issues and boost expertise for the clinical application of nanomedicine.

Ensuring the Responsiveness of Regulatory Policies

The Regulation Working Group has identified the following approaches as important steps to ensure the responsiveness of regulatory policies concerning nanomedicine:

- engagement;
- regulatory partnership;
- differentiated considerations; and
- environmental, health and safety (EHS) risk management.

i. Engagement

The regulatory framework must be grounded in users' experience and regulatory policies communicated with stakeholders at early stages (see Annexes 2 and 3 for more information).

Recommendation 5

The European Commission should establish and promote early dialogue with the different stakeholders on regulatory issues concerning nanomedicine, and ensure the regulatory framework for nanomedicine is grounded in users' experience.

¹ The UK report "Nanoscience and nanotechnologies: opportunities and uncertainties", July 2004, RS Policy document 19/04, The Royal Society and The Royal Academy of Engineering, points out that "some chemicals are more toxic when in the form of nanoparticles or nanotubes ... safety assessments based on the testing of a larger form of a chemical cannot be used to infer the safety of chemicals in the form of nanoparticles". Consequently the adequacy of existing chemicals regulation should be appraised. The UK's "Overview" of regulation presents an analysis of regulatory gaps. See "An Overview of the Framework of Current Regulation affecting the Development and Marketing of Nanomaterials", Report to the UK Department of Trade and Industry, December 2006.

² The European Commission has recently updated two guidance documents: 1) MEDDEV 2.1/3 rev 3 Borderline products, drug-delivery products and medical devices incorporating, as an integral part, an ancillary medicinal substance or an ancillary human blood derivative; 2) Manual on Borderline and Classification in the Community Regulatory Framework for Medical Devices.

³ Workplace Exposure to Nanoparticles, EASHW, 2009, based on materials published up to November 2008.

Recommendation 6

Patients' involvement in the nanomedicine policy making process should be institutionalised at both EU and national levels.

ii. Regulatory Partnership

Opportunities for companies to have early dialogue with regulatory bodies (including notifying bodies on issues concerning what data would be considered appropriate and sufficient) will contribute significantly to regulatory clarity and facilitate mutual learning on the nature of the data required. Such a process will encourage the development of consensus about data to be generated and shared, therefore facilitating progress towards licensing.

Recommendation 7

The European Commission should facilitate the accessibility of regulatory expertise by establishing user-friendly mechanisms which encourage early dialogue with regulatory bodies and regulatory partnership in order to facilitate consensus on data requirements.

iii. Differentiated Considerations

The Regulation Working Group has concerns regarding the capacity of national regulatory authorities and the need for differentiated policy considerations.

Recommendation 8

The European Commission should:

- consider the appropriate application of the subsidiarity principle in regulating nanomedicine, taking into consideration national regulatory infrastructures and cultures. The need for capacity building at national level should also be addressed in EU regulatory policy.
- ensure regulatory policies take into account factors such as the situation in different Member States, different sizes of companies and different types and applications of nanotechnologies.

iv. Environmental, Health and Safety (EHS) Risk Management

The safety of workers who may have the most exposure to nanomaterials is a major focus for regulation. This has been addressed in a comprehensive recent report by the European Agency for Safety and Health at Work⁴. The current principles of risk assessment are judged to be in general appropriate. However, the validation of in vitro methods and the development of a testing strategy remain future tasks. Classification and labelling as well as occupational exposure limits, which are derived from toxicological data, are

appropriate instruments for managing risks resulting from exposure to nanomaterials. Critically, however, these depend on the availability of toxicity studies.

A review of the recent literature on workplace exposure to nanoparticles indicates that several statutory instruments are in place to ensure an appropriate level of protection of workers. Currently there is discussion of how to consider appropriately the broad variety of nanomaterials within these regulations.

In addition, the Community strategy on health and safety at work for the period 2007 – 2012 includes nanotechnology as an important topic to be worked on in the context of the identification of new, emerging risks, and specific topics have been identified as priorities for future actions and activities.

Hospitals and nanotechnology companies have responsibility for their workers' safety. Evidence from around the world suggests wide diversity in the standards expected or imposed, but intense reporting and electronic media maintain a continuing pressure for improvement, if not conformity. Medical waste disposal procedures normally have to follow very strict regulation. However, the environmental impact of medical waste is a relatively new topic in regulation, and is characterised by many unknowns. The Working Group believes that most of the hospitals that are working with nanomaterials are not aware of their potential environmental impacts.

Recommendation 9

The European Commission should ensure continued efforts to address and monitor the health and environmental impact of nanomedicine, including improving awareness of environmental, health and safety (EHS) issues of nanomaterials, both in hospitals and nanomedicine companies.

Establishing Mechanisms of Credibility for Responsible Innovation

Given the hype about new technologies, and both the anxieties and over-expectations that the general public may have as a result, there is a need for society to establish and promote mechanisms that offer credibility and authority. This supports and encourages responsible practice in the development of innovative products. Institutional mechanisms that facilitate a common perspective with regard to clarity, objectivity, and common practice for credibility and authority will help to guide and facilitate responsible innovation.

Recommendation 10

The European Commission should support institutional mechanisms that facilitate a common perspective with regard to clarity, objectivity, and common practice for credibility and authority, e.g. joint efforts on development of testing protocols, standards and best practice.

The Economic Implications of Regulation

Regulation has significant economic implications for companies' competitiveness and the availability of products. It is therefore important to find the balance between patients' need for speedy access to innovative medical products and society's general need for safety.

For example, on the one hand the expensive high stringency classification (class III) may have a significant impact on small and medium-sized enterprises' (SMEs) research and development strategies and investments in beneficial products with niche markets. On the other hand, the assessment of biological and medical devices that is based on the application of voluntary or general (non-specific) standards may not be sufficient to address the safety issues of borderline products.

For SMEs, access to regulatory expertise and the cost of meeting regulatory requirements present significant barriers to bringing innovative and potentially beneficial nanomedicine products to market.

Regulation also has considerable impact on the insurability of environmental, health and safety risks and legal risk such as liability involved in the development of nanomedicine. In light of what the insurance industry has learned to date through monitoring activities, it would appear that there is currently no urgent need to tighten underwriting. Nor, however, should one sound the 'all clear'. Nanotechnology, in its immense diversity, is developing rapidly. While current questions as to its potential risks will be answered, new ones will also emerge (see Annex 4 for more information).

Recommendation 11

Regulators should take into consideration the economic implications of regulation for nanomedicine, including impact on timeline, insurability and the funding support needed for access to regulatory expertise and extra compliance investment, especially for SMEs and academic institutions.

Looking to the Future: Ensuring a Proportionate Approach

This report draws on a wide range of literature surveyed, and a broad spectrum of conclusions advocated by different authors or groups. However, **it is important to recognise that the situation is evolving continuously, with the progress worldwide of scientific knowledge, and the continuing efforts to bring the new knowledge into application in various fields.** Hazards may exist in some research activities, and in some applications: risk management suggests the use of "appropriate" regulations, which covers several possibilities:

- It may be that existing regulations can be interpreted to cover the new, nanotechnological application, even if there is no explicit language covering the specific use. It would be unhelpful (although unfortunately not unprecedented) for regulations to be drafted in great detail, as such regulation carries the risk of rapid obsolescence, and inhibits research and innovation.
- At the opposite extreme from over-detailed regulations, there is the simple possibility of a general moratorium. This is quickly drafted, and apparently a "safe option" – if only one side of the safety balance is considered. However, it has maximal adverse effect on incentives for research and innovation, and clearly reduces or eliminates a country's ability to compete in the new sectors and activities which may be opened up by the progress of knowledge and technique. The history of the over-regulation of genetically modified organisms (GMOs) in the EU provides an example. The report endorsed by the European Parliament in April 2009 appears to tend in this direction: it is based on extensive research, which in political debate becomes reduced to the simplistic, memorable (and potentially dangerous) formula (used in the debate on REACH) of "no data, no market".

The Regulation Working Group concludes that, while some regulation is clearly necessary, it should be applied proportionately and limitedly. New legislation may well not be required if the situations arising can be covered by intelligent interpretation of existing texts, and/or standards, codes of practice, guidelines, and informal but enforceable agreements. The concept of proportionateness and limitation may include:

- the concept of "case-by-case" decisions, and monitory oversight, to facilitate learning;
- the use of "sunset clauses" to end or adapt regulations if not explicitly renewed.

⁴ The general framework is provided by the regulation on occupational safety and health of workers (EU Directive 89/391/EEC) and specifically for chemical safety by the directive on the protection of the health and safety of workers from the risks related to chemical agents at work (Directive 98/24/EC). Substance-specific regulation is intended by the biocide Directive (Directive 98/8/EC) and Regulation 1907/2006 (REACH).

⁵ European Parliament, report on regulatory aspects of nanomaterials (2008/2208(INI)).

Communication and Understanding of Nanomedicine

Report by the Patients' Needs Working Group of the NanoMed Round Table

Summary and Recommendations

KEY POINTS

Public engagement and deliberation about nanomedicine at all levels is fundamental if we as a society want to profit from the hopes and promises invested in nanomedicine.

Credible and accessible sources of balanced information must be provided, together with fora to debate and discuss questions about needs, risks, benefits and ethical and social issues relating to nanomedicine to facilitate understanding and dialogue.

Communications know-how needs to be fostered among nanomedicine stakeholders, otherwise the development, introduction and application of innovative nanomedical treatments will be significantly delayed or hindered.

Good communication needs adequate financing – this should be built into all nanomedicine funding.



Defining Nanomedicine and Communication

There is much uncertainty in defining the term 'nanomedicine', not least because this relatively new field is transdisciplinary, blurring established boundaries and combining previously unconnected fields. When considering this report's recommendations this uncertainty must be taken into account, as public engagement and deliberation can only be effective if there is agreement on a common foundation on which to build dialogue.

For the purpose of this report 'communication' also needs to be defined. The goal of any nanomedicine communication strategy must be to initiate public debate, deliberating on both personal and social consequences of innovations and acknowledging that a simple discussion of risks and benefits should only be a starting point for dealing with the complex concerns of a technology-dependent society. Furthermore, the communication requirements of individual members of the public can greatly differ, so it is vital for any successful communication strategy to take the range of understandings and expectations into account.

The Importance of Communicating About Nanomedicine
Communicating about nanomedicine is increasingly important because of its significant potential to:

- raise societal and ethical questions concerning risks and benefits; and

- have an emotional and material impact (arising from benefits and uncertainties) due to the large number of people affected.

However, there is still a considerable lack of public awareness about nanomedicine. At the same time, social, ethical and legal questions are being raised concerning safety, environmental and long-term effects. The best way to answer the demands of an inquiring public is to develop and implement a strategic approach for active public debate.

Any communication strategy needs to take into account the significant changes in communication methods; for example, the internet and new media are replacing doctors as the primary source of medical information. Communication practices must therefore be continuously innovative in order to reach as wide and varied an audience as possible.

Providing Reliable Information About Nanomedicine
In order to enable patients to make informed decisions, the public needs access to reliable and credible sources of information and fora to debate and discuss questions about needs, risks and benefits as well as ethical and social issues related to nanomedicine.

Recommendation 1

The European Commission should establish a platform to provide credible and accessible sources of balanced information on the methods, benefits and risks of nanomedicine, focusing on the communication needs of patients and the medical community.

Establishing such a platform would make it easier for the public to understand fundamental nanomedical issues, and would also support the communication tasks of stakeholders such as doctors, patient groups and health insurers.

Providing Know-How for Communication About Nanomedicine

The majority of current nanomedical research and development is conducted by small or medium-sized enterprises (SMEs) which often do not have the know-how, staff time and financial resources required for initiating and implementing successful communication strategies. This can significantly delay or hinder the development, introduction and application of innovative nanomedical treatments, to the detriment of nanomedicine's medical and economic impact in Europe.

The communication aspects of the related fields of food and environment must be carefully differentiated, or negative tendencies concerning these fields may have detrimental effects on nanomedicine.

Recommendation 2

The European Commission should develop communication guidelines for the various nanomedicine stakeholders and provide good practice examples. Particular care should be taken to differentiate between the communication aspects of the related fields of food, environment and nanomedicine.

Ensuring Sufficient Resources for Communication About Nanomedicine

Inefficient or inadequate communication about nanomedicine can lead, on a small scale, to the rejection of an individual treatment method. On a larger scale, a number of such cases of rejection could lead to distrust and fear of the entire field. The question is how to finance communication in a field which is struggling to define itself and which has long development times and therefore long investment return times, meaning that profits are currently negligible.

Recommendation 3

The European Commission, national governments, industry and independent grant organisations should allocate a significant percentage of financial resources in the field of nanomedicine to public communication. The goal of this financial allocation should be to encourage public engagement, foster dialogue and move beyond the simple discussion of risks versus benefits.

Defining Nanomedicine and Communication

i. Definition of Nanomedicine for Communication Purposes

From a communication point of view it is interesting to note that neither the participants of the Set-up Round Table meeting nor the members of the Communication Working Group were able to agree on a precise definition of the term 'nanomedicine'. Suggestions ranged from the simple 'application of nanosciences to medicine', through the elaborate definition used in the NanoBio-RAISE project, which differentiated between 'nanomedicine and medical nanotechnologies', to the widespread public perception of 'nanomedicine is whatever calls itself nanomedicine'.

The difficulty in agreeing on a precise definition in itself demonstrates a significant amount of uncertainty in delineating this relatively new field of medicine. One of the main reasons for this is that nanomedicine is transdisciplinary, blurring established boundaries and combining previously unconnected fields.

When considering this report's recommendations this uncertainty has to be taken into account, as public engagement and deliberation can only be effective if the

various parties can agree on a common foundation on which to commence a dialogue. This basic tenet also applies to other issues. The Working Group deemed one potential source of disagreement to be the discrepancy between nanomedical visions and the current state-of-the-art. The hopes and expectations raised by the former are generally in no way likely to be met by the latter. However, instead of viewing this in a negative light, it should be regarded as a possible starting point for a public deliberation on nanomedicine.

The necessity for using the term 'nanomedicine' may need to be questioned. For researchers and companies the use of this term can be very important, as it can help in fund-raising, marketing, product placement or the establishment of a corporate identity, among many things. At the other end of the scale the individual patient is mainly interested in the effectiveness of a therapy ('Does it work?'), and whether it can be used to treat the patient's condition ('Will it work for me?'). At this point the 'nanomedicine' terminology of a novel therapeutic method becomes a minor concern. For patients, the difficulties of defining and delineating nanomedicine are therefore no longer an issue, which leads to the question of whether efforts to initiate and conduct a public debate based on the term 'nanomedicine' are superfluous.

ii. Defining Communication

For the purpose of this report, 'communication' needs to be considered comprehensively. The simple act of transmitting and exchanging information by various means has been extensively shown to be insufficient to address current needs. The desired outcome of nanomedicine communication should not simply be one of maximising the benefits to society whilst minimising the risks. The debate should also be reconfigured so that it better characterises what is at stake in emerging technologies.

As the DEEPEN project report states: "lay reactions to nanotechnology are complex. Public responses to the technology, or even to particular applications, are not simply either positive or negative; rather, pros and cons are seen as intermingled and often inseparable. Laypeople are also not content with weighing up risks and benefits. Their concerns and enthusiasms go beyond this narrow framing to encompass anything from the dangers of perfection to the problematic nature of controlling life."

The goal of any nanomedicine communication strategy must therefore be to initiate public debate, deliberating on both personal and social consequences of innovations and acknowledging that a simple discussion of risks and benefits should only be regarded as a starting point for dealing with the complex concerns of a technology-dependent society.

and stakeholders will themselves have different definitions of the term 'communication'. In the extreme the term could mean things as distant as propaganda and education. It is therefore essential to separate, for example:

- communication with peers/industry/students/policy makers (a form of marketing with science: seduce, sell, convince);
- communication with the media (inform, avoid sensationalism); or
- communication with the public (explain, evaluate, debate, deliberate).

These different definitions have to be kept in mind when discussing and planning a comprehensive communication strategy in order to avoid misunderstandings between the various stakeholders. It is also essential to take into account the communication requirements and needs of the various stakeholder groups. For example, various studies, including that conducted by the NanoMed Round Table's Patients' Needs Working Group, have shown that the level of knowledge about nanomedicine is very low among the public in general.

It is also important to note that **the communication requirements of each individual member of the general public can greatly differ**, ranging from the simple request for basic information on a specific therapy to a need for fully-fledged deliberation on ethical, social and regulatory aspects. **It is therefore vital for any successful communication strategy to take this range of varying expectations into account.**

Ensuring Reliable and Responsible Communication About Nanomedicine

The findings and recommendations in this report are based on a thorough analysis of existing case studies, documents, and construction of scenarios on the possible consequences and impacts of various communication methods in the field of nanomedicine. The Working Group's discussions were focused around two main case studies chosen for their wide range of communication aspects:

- the communication strategy of the nanomedical company 'MagForce Nanotechnologies AG' (see Annex 1); and
- a study of 'Visions of Nanomedicine' (see Annex 2).

The Working Group also took into account patients' needs and ethical, regulatory, social and economic issues.

i. The Importance of Communicating About Nanomedicine

Communicating about nanomedicine is increasingly important because of its significant potential to:

- raise societal and ethical questions concerning risks and benefits due to the predicted use of active nanomaterials in novel treatments and, subsequently, their use within the human body; and
- have an emotional and material impact (arising from benefits and uncertainties) due to the large number of immediately and peripherally affected people.

Although the term 'nanomedicine' has been used by experts and stakeholders to describe the application of nanotechnology to health and medicine for over ten years, there is still a considerable lack of public awareness concerning this field. Despite high expectations of future developments to enable better, more efficient and affordable healthcare for millions of patients and promise novel treatments for many illnesses, the general public is often uninformed not only of these potential benefits, but of the entire field of nanomedicine.

However, even among informed members of the public, perceptions vary significantly. On the one hand the abundance of visions, both realistic and unrealistic, has raised hopes which stakeholders may well not be able to meet in the near future, due to the time required for the development and marketing of novel treatment methods. At the same time, social, ethical and legal questions are being raised concerning issues of safety, environmental and long-term effects, to name but a few. In particular, the use of treatments based on active nanomaterials such as therapies with cancer-targeting particles or theranostic approaches have high potential for controversy. **The best way of answering the demands of an inquiring public is to realise the need for active public debate and to develop and implement strategic approaches to this end.**

The potential of nanomedicine to be the field of application about which important societal and ethical questions are first raised, means that **any public reaction to nanomedicine is likely to reflect on nanotechnological applications outside of the medical field**. However, one of the inherent dangers is that the nanomedical community will not be able to fulfil the expectations of a hopeful public before it becomes disillusioned. **A comprehensive debate on the visions, likely timelines, risks and benefits of nanomedicine is, therefore, also vital to the future of nanotechnology.**

Although easy to state and recommend, facilitating such a comprehensive debate is not a trivial task. Public engagement is challenging, and reactions can often differ greatly from the desired outcome. It is therefore necessary to work to

understand the complexity of public 'attitudes' and to continuously adapt communication strategies accordingly.

As expert groups and governments have repeatedly stated, it is also important for scientists, businesses and other stakeholders to 'earn' public trust in order to be able successfully to engage the public in dialogue, for example on how to develop and regulate nanotechnologies.

Furthermore, there is a need for governments and funders across Europe to respond to past public dialogues and expert group recommendations in order to prevent overreactions to potential hazards and risks, which would severely limit the possibility of public dialogue and potentially lead to the whole area of nanotechnologies being rejected by the public and NGOs. In view of this, special attention should be paid to communication in the fields of health and environmental impacts of nanoparticles, as substantial amounts of funding go into commercialising them.

Finally, any communication strategy that is developed needs to take into account the significant changes in communication methods that have occurred over the past years. For example, the importance of doctors as the primary source of medical information is steadily declining, being replaced by the internet and new media. This development is questionable, as the quality of this information is highly variable on the one hand, whilst on the other hand the sheer volume of information is often confusing or overwhelming to the average patient. Both these aspects can lead to confusion and misunderstanding. Nevertheless it is expected that patients give their informed consent before initiating a medical treatment, often based on this confusing or overwhelming information. This is a discrepancy which needs to be addressed. **In order to enable patients to make informed decisions, the public not only needs access to a reliable and credible source of information, but also to fora to debate and discuss questions concerning needs, risks, benefits, as well as ethical and social issues related to nanomedicine.**

In conclusion, it is therefore important to be continuously innovative in communication practices, especially pertaining to public engagement and debate, in order to reach as wide and varied an audience as possible.

ii. Providing Reliable Information About Nanomedicine

Recommendation 1

The European Commission should establish a platform to provide credible and accessible sources of balanced information on the methods, benefits and risks of nanomedicine, focusing on the communication needs of patients and the medical community.

¹ Davies, S., Macnaghten, P. and Kearnes, M. (ed.) 2009. Reconfiguring Responsibility: Lessons for Public Policy (Part 1 of the report on Deepening Debate on Nanotechnology). Durham: Durham University.

² Ref. Patients' Needs Working Group report.

³ Combined diagnosis and treatment.

The term 'nanomedicine' is a generic term and can therefore generate misunderstanding, which is a source of mistrust and doubt. Even experts find it difficult, if not impossible, to provide a valid and accepted definition for this term. In addition, lay people often become confused by the wealth of information available and unspecified use of technical terms. This also leads to uncertainty and apprehension. Recommendation 1 is intended to help achieve higher clarity of message in regard to nanomedicine, and therefore counter these problems.

The platform should provide quality information whilst also encouraging public debate and deliberation on risks, innovations and developments in the field of nanomedicine. It should focus on the communication needs of those most immediately and personally affected by nanomedicine: patients, doctors, healthcare workers, medical students and pharmacists.

Prior to establishing the platform, representatives of the groups listed above need to be consulted to determine their needs concerning required information, dialogue fora and interactive elements. The inclusion of certain stakeholder groups at such an early stage correlates with the findings of the Patients' Needs Working Group, which recommended a communication loop where patients could contribute what they would like to know and how they would like this information to be structured and made available. At a secondary level, further stakeholders should be included such as health insurers, regulatory bodies and pharmaceutical companies.

In order to ensure that the format of the platform remains up-to-date with new developments, both with regard to the nanomedical field as well as to public debates, the platform should be reviewed every two or three years. The review, which could be organised as a recurring round table event, should involve various stakeholders and a wide range of experts in the fields of nanomedicine, communication, ethical and social debate, as well as representatives of doctor and patient organisations. As an additional benefit this approach could provide a model for other medical fields such as regenerative medicine.

Establishing such a platform would not only make it easier for the general public to understand fundamental nanomedical issues as well as specific product details, but would also support the communication tasks of key actors in this field such as doctors, patient groups and health insurers.

A structured communication platform in the nanomedical field would contribute to the improvement of sub-optimal communication between health professionals, which is a significant cause of incidents compromising patient safety. It

⁴ Ref Patients' Needs Working Group report.

⁵ Recommendation 2 - The European Commission has produced much useful information on the internet on nanotechnology aimed at the general public, e.g. short films, leaflets and brochures. It should organise the production of similar lay information on nanomedicine, which could be used by patient organisations, clinicians and the media.

would alleviate current problems of information transfer, thereby reducing future misunderstandings. This will become increasingly important as nanomedical methods become more complex and the associated communication issues become increasingly challenging as a result.

Recommendation 1 would also satisfy a number of important points raised by the experts involved in the NanoMed Round Table project, not least because it could be used to implement some of the Patients' Needs Working Group's recommendations. In the initial phase Recommendations 7 and 8 should be considered, whilst the information referred to in Recommendations 2 and 3 could be incorporated into the final platform.

iii. Providing Know-How for Communication About Nanomedicine

Recommendation 2

The European Commission should develop communication guidelines for the various nanomedicine stakeholders and provide good practice examples. Particular care should be taken to differentiate between the communication aspects of the related fields of food, environment and nanomedicine.

Common questions concerning the subject of nanomedicine are not only 'How does it work?' or 'What are the risks?', but also 'How reliable is the information?', 'How do they know?', 'Who is the messenger?' or 'Can the messenger be trusted?'

The latter five questions are directly linked to the expectations of the questioner, and can therefore directly influence acceptance, so **a structured communication strategy is vital to improving public understanding of and initiating a balanced public dialogue on nanomedicine.** In addition, due to their individuality, highly specialised nanomedical treatments will often require specifically tailored communication approaches. This is also often necessary due to competition, alternative treatments, patient needs and numerous other reasons.

However, as the majority of current nanomedical research and development is being conducted by small or medium-sized enterprises (SMEs), **the actors in this field often do not have the know-how or staff time and financial resources**

Recommendation 3 - European-level trade and research associations should produce lay information using stakeholder dialogue on nanomedicine research. National-level trade and research associations should disseminate this information in their country's language(s) to patient organisations, media and bodies representing clinicians. The European Commission should investigate what existing programmes should or could fund this, and/or develop new funding streams where required, e.g. science and society programmes or European Science Foundation.

Recommendation 7 - Where governments have organised stakeholder fora to discuss the potential risks and benefits of nanotechnologies including nanomedicine, they should encourage patient organisations to participate. Where such fora do not exist, governments should urgently consider establishing them.

Recommendation 8 - The European Commission should provide funding for focus groups and other participatory methods (e.g. citizen conferences, interviews, surveys) in a number of European countries, to identify and understand the spectrum of issues that nanomedicine raises for patients and their families.

required for initiating and implementing a successful communication strategy. This can significantly delay or hinder the development, introduction and application of innovative nanomedical treatments, with a detrimental effect on the impact of nanomedicine in Europe, both in medical and economic terms.

For the above reasons, a series of communication guidelines should be developed by leading experts in this field. These could be used by research organisations, nanomedicine companies and other stakeholders as an effective tool for initiating public engagement whilst contributing to economic viability. The guidelines could be compiled in the form of a matrix, containing information on:

- which target groups need to be communicated to (e.g. regulatory bodies, patient groups, medical associations, general public, NGOs);
- what information is required by these individual groups (e.g. technical requirements, regulatory issues, possible side effects, life cycle analysis); and
- at what stage of treatment, development or testing the required information should be communicated to the respective groups.

In developing these guidelines **a special emphasis must be placed on carefully differentiating between the communication aspects of the related fields of food, environment and nanomedicine.** Although there are some common issues and overlap in certain areas, it is highly important that the differences of these respective fields are communicated. **If this is not considered, any negative tendencies concerning nanotechnology in food or environment are likely to have detrimental effects on the field of nanomedicine.**

However, the development and application of communication guidelines does not in itself guarantee the success of a nanomedical method or even of nanomedicine itself. The case study on MagForce Nanotechnologies (see Annex 1) shows that even a principally sound communication structure is in itself not sufficient to ensure a breakthrough of a novel treatment (obviously one of the main goals for a company developing a new product). In this case the company was not able to convince the professional oncology community to support the development of their treatment method, despite promising test results. This hindered the project, influencing the choice of test subjects and causing delays in the clinical tests.

iv. Ensuring Sufficient Resources for Communication About Nanomedicine

Recommendation 3

The European Commission, national governments, industry and independent grant organisations should allocate a significant percentage of financial resources in the field of nanomedicine to public communication. The goal of this

financial allocation should be to encourage public engagement, foster dialogue and move beyond the simple discussion of risks versus benefits.

Communication is one of the main pillars of our society. Good communication causes societies to flourish, businesses to prosper and innovations to succeed. In contrast, inefficient or inadequate communication is a major source of doubt, distrust and fear, with potentially devastating results. In the case of nanomedicine, this could lead, on a small scale, simply to the rejection of an individual treatment method. On a large scale, however, a number of such cases of rejection could lead to distrust and fear of the entire field.

A key question, however, is how to finance communication in a field which on the one hand is struggling to define itself, whilst on the other hand has long development times and therefore long investment return times, meaning that profits are negligible, currently and for the near future. In answer to this question, a significant percentage of financial resources in the field of nanomedicine should be allocated to communication – both in European and national funding programmes as well as by industry and independent grant organisations. This approach would ensure that communication expenditure is directly tied into the amount invested into research and would therefore automatically increase with any future growth in this field. In addition, the informational content would always be tied into current research, ensuring up-to-date communication.

In this context it is important to ensure that the communication strategies of a project are not simply focused on disseminating the results of the project itself. Of course this is always a vital element in any project. However, **the goal of this financial allocation should be to go many steps further, encouraging public engagement, fostering dialogue and moving beyond the simple discussion of risks versus benefits.** In practice, project proposals which do not demonstrate a comprehensive communication strategy should receive a lower evaluation or be encouraged to improve on this point. It could also be a requisite that new calls for proposals recommend the inclusion of project partners with expertise in this field.

Furthermore, businesses need encouragement and support in engaging with the public in the ways described above. At present, many nanotechnology companies are fearful of public engagement, having seen what happened regarding the issue of genetic modification, and are aiming to 'manage the message' better, rather than open up a dialogue with the public about developing nanotechnologies. Although at first this would seem to be a preferable way of preventing or limiting overreactions in this field, in the long term it is counter-productive to improving public understanding and initiating a balanced public dialogue on nanotechnology in general and nanomedicine in particular.

NanoMed Round Table Participants

Steering Committee

Chair Prof Sir John Beringer	Formerly Pro Vice-Chancellor, University of Bristol, Symbiotic Consultancy Ltd, UK
Coordinator Prof Julian Kinderlerer	TU Delft, Netherlands/ University of Cape Town, South Africa/ European Group on Ethics in Science and New Technologies
Management Dr David Bennett	Delft University of Technology, The Netherlands & St Edmund's College, University of Cambridge, UK
Dr Klaus-Michael Weltring Serene K. Chi	Bioanalytik-muenster, Germany TU Delft, Netherlands

WP2 Patients' Needs

Chair Alastair Kent	Director, Genetic Interest Group, UK
Participants Dr David Bennett	Delft University of Technology, The Netherlands & St Edmund's College, University of Cambridge, UK
Prof Dr Sir John Beringer Avril Daly Laura Gilbert Melissa Hillier Dr Mahendra Gonsalkorale Lorraine Le Floch Sabine Lobnig Rod Mitchell Liuska Sanna	Formerly Pro Vice-Chancellor, University of Bristol, Symbiotic Consultancy Ltd, UK Fighting Blindness, Ireland Rapporteur Genetic Interest Group, UK Former member of European Parkinson's Association Independent Patient, European Multiple Sclerosis Platform (EMSP) European Patients Forum Chairman, European Crohn's and Colitis Organization (ECCO) European Patients Forum

WP3 Ethical and Societal Aspects

Chair Prof Alfred Nordmann	Technische Universität Darmstadt, Germany & University of South Carolina, USA
Participants Dr Johann S. Ach Dr David Bennett	Universität Münster, Germany Delft University of Technology, The Netherlands & St Edmund's College, University of Cambridge, UK
Prof Dr Sir John Beringer Prof Marianne Boenink Dr Donald Bruce Dr Karin Christiansen Prof José Manuel de Cózar Dr Arianna Ferrari Robert Geertsma Prof Uffe Juul Jensen Jan Reinert Karlsen Prof George Khushf Dr Thorsten Kohl Dr Ineke Malsch Dr Sabine Müller Prof João Arriscado Nunes Prof Jan Helge Solbakk Prof Mariachiara Tallachini Dr Susana Vidal Dr Klaus-Michael Weltring	Formerly Pro Vice-Chancellor, University of Bristol, Symbiotic Consultancy Ltd, UK University of Twente, Netherlands Edinethics Ltd., Edinburgh, Scotland University of Aarhus, Denmark University of La Laguna, Spain Technische Universität Darmstadt, Germany RIVM Bilthoven, Netherlands University of Aarhus, Denmark University of Oslo, Norway University of South Carolina, USA Technische Universität Darmstadt, Germany (Researcher, Rapporteur) Malsch TechnoValuation, Netherlands Universität Bonn, Germany University of Coimbra, Portugal University of Oslo, Norway University of Milano, Italy UNESCO, Uruguay Bioanalytik-muenster, Germany

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WP4 Economic Impact

Chair Dr Françoise Charbit	CEA, France
Participants Dr François Berger Prof Dr Sir John Beringer Dr Bernhard Buehrlen Dr Giorgio Cassara Dr Paul Garassus Dr Laurent Levy Dr Christine M'rini Dr Christine Muzel Prof Reinhard Rychlik Dr Jürgen Schneckeburger Dr Paul Smit Dr Klaus-Michael Weltring	Grenoble Hospital and INSERM, France Formerly Pro Vice-Chancellor, University of Bristol, Symbiotic Consultancy Ltd, UK Fraunhofer Institute for Systems and Innovation Research, Germany Don Gnocchi Foundation, Italy Clinique du Tonkin, France Nanobiotix, France Mérieux Alliance, France Philips Healthcare, Netherlands Institute for Empirical Health Economics, Burscheid, Germany University Clinic Münster, Germany Philips Healthcare, Netherlands Bioanalytik-muenster, Germany

WP5 Regulation

Chair Mark Cantley	Formerly European Commission Research Directorate-General, UK
Participants Prof John Adams Dr Mike Adcock Prof Dr Sir John Beringer Serene K. Chi Prof Ken Donaldson Dr Bärbel Dorbeck-Jung Joel D'Silva Dr Thomas K. Epprecht Dr Steffi Friedrichs Dr Peter Hatto Dr Juergen Hirschfeld Dr Peter Kearns Prof Julian Kinderlerer	University College London, UK Durham University, UK Formerly Pro Vice-Chancellor, University of Bristol, Symbiotic Consultancy Ltd, UK Delft University of Technology, The Netherlands University of Edinburgh, UK University of Twente, Netherlands Leuven University, Belgium Swiss Re, Switzerland Nanotechnology Industry Association, Belgium CEN/ISO, UK Bayer, Germany OECD, France Delft University of Technology, The Netherlands/ University of Cape Town, South Africa/ European Group on Ethics in Science and New Technologies Siemens, Germany University of Lisbon, Portugal Philips, Netherlands Bioanalytik-muenster, Germany Chinese Academy of Science, China
Dr Horst Siebold Prof Rogério Sá Gaspar Dr Rob Slobbe Dr Klaus-Michael Weltring Dr Jiang Yu	

NanoMed Round Table Participants

WP6 Communication

Chair

Prof Dr Wolfgang M. Heckl Deutsches Museum/ TU München, Germany

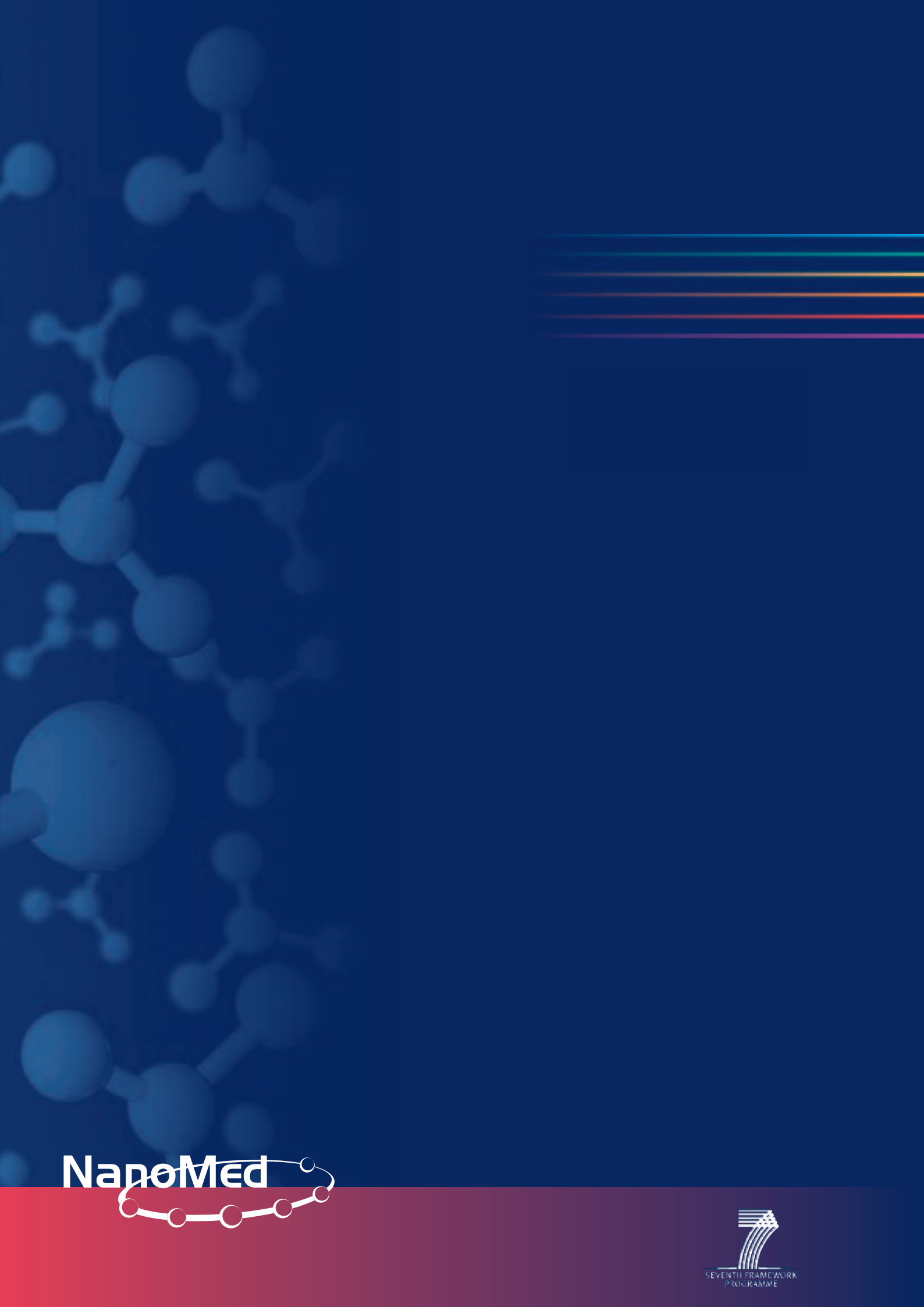
Participants

Dr David Bennett of Cambridge, UK
Delft University of Technology, The Netherlands & St Edmund's College, University of Cambridge, UK
Prof Dr Sir John Beringer
Formerly Pro Vice-Chancellor of University of Bristol, Symbiotic Consultancy Ltd, UK
Mark Cantley
Formerly DG Research, UK
Richard Hayhurst
Hayhurst Media, UK
Melissa Hillier
Genetic Interest Group, UK
Paul Hix
Deutsches Museum, Germany
Dr Andreas Jordan
MagForce Nanotechnologies AG, Germany
Dr Ulrich Kernbach
Deutsches Museum, Germany
Prof Dr Harald Krug
EMPA Materials Science & Technology, Switzerland
Prof Dr Phil Macnaghten
Durham University, UK
Hayley Birch
Science Writer/Editor, UK
Prof Dr Harald Fuchs
WWU Münster, Germany
Dr Antje Grobe
Risk Dialogue Foundation, Switzerland
Prof Kathy Sykes
University of Bristol, UK
Wiebke Pohler
LMU München, Germany
Dr Michael Schillmeier
LMU München, Germany
Bart Walhout
Rathenau Institute, Netherlands
Dr Klaus-Michael Weltring
Bioanalytik-muenster, Germany

Other Contributors

Dr Simon Baconnier
Connective Tissue Cancer Network, France
Dr Bruno Bonnemain
Guerbet, France
Prof Gérard Duru
University of Lyon, France
Dr Philippe Mourouga
Sanofi Aventis, France
Dr Detlef Niese
Novartis, Switzerland
Prof Dr Lode Vereeck
Member of the Flemish Parliament, Belgium





NanoMed

The logo graphic for NanoMed consists of a white line that starts below the 'N', curves under the 'o', and then continues under the 'M' and 'e'. Along this line, there are several small white circles of varying sizes, some of which are connected to the line, suggesting a molecular or network structure.