



Nanobioethics

ObservatoryNano 2nd Annual Report on Ethical and Societal Aspects of Nanotechnology

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Executive summary

In the areas of nanobioethics and nanobiotechnology and society, the scientific, public and philosophical and social science debates circulate around five topics: Human Enhancement, Synthetic Biology, Nanomedicine, Agrifood and Animal Testing. These focus areas emerge in policy and stakeholder debate on nanotechnology for health, medicine and biotechnology and nanotechnology for agrifood, two of the ten technology sectors where nanotechnology is being applied which are analysed in the ObservatoryNano project. The assessment in this report is organised from the broadest (human enhancement and synthetic biology) to the narrowest debates (animal testing).

The concepts Human Enhancement and Synthetic Biology have given rise to more general ethical and societal issues discussed by policy makers and stakeholders as well as philosophers and social scientists. Some trends in nanotechnology for Health, Medicine and Biotechnology may have implications for human enhancement or synthetic biology. One aim of the present report is to contribute to better societal embedding of these technologies and their applications. Nanoscientists involved in such research for medical or other purposes do not always take into account the issues in those wider debates. Policy makers, stakeholders and social scientists are not always aware of the actual scientific developments and their implications. They run the risk of discussing only mere science fiction scenarios.¹ Both Human Enhancement and Synthetic Biology have strong dual use potential, including military as well as civilian applications. The civilian applications are broader than healthcare, and include sports and cosmetics. In both cases, widening the divide between rich and poor countries and groups in society is among the major concerns.

There is a current political and stakeholder debate on human enhancement at EU level and in several countries. Especially in the area of Human Enhancement Technologies in Sports, there are initiatives to install Parliamentary bodies for monitoring the developments and governing the developments. Nanotechnology may be applied in some human enhancement technologies, including preventive healthcare and regenerative medicine. Current issues in the philosophical and ethical debate include risks, implications for human self-perception and concepts like health and disability, social injustices, competition spiral and degradation of social norms and values. Incremental and radical enhancements are distinguished, and several authors recommend focusing the debate on short to medium term developments rather than very futuristic scenarios. New issues for debate include different concepts for discussing the human condition and religious viewpoints on human enhancement.

Even though most issues in the current debate on synthetic biology are not related to nanotechnology, some trends in nanobiotechnology may also be affected by the policy measures suggested by the European Group on Ethics and others. The safety of workers in multidisciplinary research labs and of amateur scientists requires constant attention. Governance of intellectual property of new technologies including nanobiotechnology could also benefit from new ideas proposed by the European Group on Ethics and other experts. The EU Code of Conduct for Nanotechnology Research (2008) could serve as an example for a code of conduct for synthetic biology as proposed by EGE. Philosophers reflecting on attempts at creating artificial life place nanotechnology and synthetic biology in a century old tradition in natural sciences to mimic or improve nature. They raise ethical questions like: should everything that scientists are capable of, be allowed?

¹ Anticipation of likely future developments including technological as well as societal trends is necessary, but future visions should not be disconnected from actual relevant technological and societal developments.

Nanomedicine is a key area of nanotechnology, with a lot of research activity as well as debates about ethical and societal aspects. At least in Europe, three sub domains are the priorities for public and private investment: nanopharmaceuticals, diagnostics and regenerative medicine. Neuronanoscience may in the future become a fourth research priority in Europe. The stakeholder debate focuses mainly on socio-economic issues such as how to improve Europe's competitiveness in nanomedicine or nanobiotechnology in general and on how to make available balanced information for medical professionals and patients. The Nanomed Roundtable made the following recommendations to the European Commission and national governments. The deliberation of ethical and societal issues should be complemented with consideration of the feasibility of particular nanomedicine developments. This should be done by assessment of the visions driving nanotechnological developments as well as analyses of relevant cultural, societal and commercial trends. Current issues discussed in ethical and social science literature which should be discussed in broader forums include autonomy and privacy issues related to personalised medicine and access to nanomedicine for deprived populations. In general, there are six areas of relevant ethical issues, including risk assessment in medical research, diagnosis and therapy, questions of personal and human identity, enhancement by possible nanotechnological implants, distribution of risks and potential benefits, which groups are included in clinical trials, and the potential need for rethinking the traditional model of the patient-physician relationship. Philosophers see the need to engage with embedded notions of health, disease, molecular medicine etc and with the normativity of these concepts.

Nanotechnology in agrifood is a separate area. Whereas according to some experts nanotechnology has the potential to contribute to food safety & security, sustainable use of resources and animal welfare, this is contested by others. Stakeholder concerns include consumer choice and transparency regarding products and processes using nanotechnology in the food sector. NGO's are concerned about the absence of nano-specific safety laws and the lack of public involvement in decision making. Political decision making on nanotechnology in novel foods and nano-labelling of food products is in progress in Europe, but controversies appear to remain especially related to the novel food regulation.

Ethicists and social scientists explored similarities and differences of nanotechnology and GMO's in agrifood. The different stakeholders discussing nanotechnology have contending perspectives on how their introduction should be governed. Company's fear of a potential public backlash may inhibit nanotechnology innovation in agriculture and food. The trend that government regulation is increasingly replaced by governance involving debates by stakeholders may have unforeseen societal consequences. Nanotechnology for agrifood applications raises particular privacy issues related to RFID chips and other remotely readable tags for cattle (privacy of the owner) and food products (consumer privacy). New hazards in the form of nano(eco)toxicity may also be introduced. There is a discussion whether animal welfare would be served by modifying animal properties or incorporating sensors and devices in the animal body.

An ethical framework for agricultural technologies proposed by the European Group on Ethics could be used to stimulate balanced reflection on ethical issues of nanotechnology for agrifood applications. Different ethical traditions including consequentialism, deontology, virtue ethics and agrarian ethics could also be useful for this.

Nanotechnology may lead to increasing as well as decreasing the need for animal testing in research. The stakeholder debate on nanotechnology and animal testing is currently not very polarised, but in the future animal rights groups may require more effort in developing alternatives for animal testing.

The choice made in this report to focus on discussions closely related to current developments in nanotechnology for medical, biological and agrifood applications makes the findings of this report useful for reflection on choices by the scientific community and policy makers in science and

technology policy dealing with nanotechnology. It is less suitable for decision making on priorities in public policies aimed at governing the society as a whole and targeting (nano)science, technology and innovation policy towards the long term sustainable and equitable development of our European and global societies.

Introduction

This report examines current trends in the co-evolution of nanotechnology and society related to nanobioethics. Nanobioethics can be considered a sub area of nanoethics dealing with biomedical, biotechnological or agrifood applications of nanotechnology. It can also be considered a sub area of bioethics where nanotechnology plays a role. In this report, nanobioethics is interpreted broader, including ethical, legal and societal aspects as well as philosophical ethics. The aim of the report is to highlight new or persistent issues currently in debate which merit the attention of politicians and policy makers engaged in decision making on Nanotechnology for Health, Nanomedicine and Nanobiotechnology as well as Nanotechnology for Agrifood applications. The report is not intended to present a new vision of the ObservatoryNano project on these issues, but to identify significant issues and views discussed by others.

The sectors covered in this report are two of the ten technology sectors where nanotechnology is being applied which are analysed in the ObservatoryNano project. The other sectors are Aerospace, Automotive & Transport, Chemistry & Materials, Construction, Energy, Environment, Information & Communication, Security and Textiles. Some of these areas have given rise to specific ethical or societal issues discussed by policy makers and stakeholders or in the philosophical and social science literature. These include the topics of this year's annual report: on Health, Medicine & Biotechnology, and Agrifood. Next year's report will focus on Ethical and Societal Aspects of Nanotechnology for ICT and Security. The other reports in this series on ethical and societal aspects of nanotechnology focus on more general issues including responsible development of nanotechnology (1st annual report) and communicating nanoethics (4th annual report). Ethical aspects of risk governance for engineered nanomaterials and cosmetics are covered in the first report. The report will be made available to European policy makers on nanotechnology and others via the website www.observatorynano.org.

The authors of this report choose to discuss ethical issues related to nanobiotechnology from the point of view of a technical vision, because the role of the ObservatoryNano is primarily to make information on non-military technological and economical trends in nanotechnology and their broader implications available to policy makers. This means selecting the S&T areas in which R&D is being done in relation to the organism (human, animal, ecosystem). It should be noted that this is one particular methodological approach. In an equally valid approach, one could choose to take the ethical and social consequences of R&D of nanobiotechnology as starting point, leading to a completely different classification (e.g. military, monopoly, concentration of wealth, labour qualification, etc.) The European Union does not fund military research under the Framework Programme for RTD and therefore also no research into societal aspects of military research (except dual use technologies). This is the responsibility of the EU Member States and the European Defence Agency (EDA). In next year's report, Ethical and Societal Aspects of Nanotechnology, ICT and Security will be discussed, including civil security and dual use applications of nanotechnology.

In this general domain of nanobioethics, current debates are circulating around five topics: human enhancement, synthetic biology, nanomedicine, agrifood and animal testing. At the political and stakeholder level, there are ongoing debates on human enhancement and on synthetic biology.² Even though both debates are broader than nanotechnology related trends, some applications of nanotechnology are relevant to human enhancement or to synthetic biology. Therefore, some of the

² It should be noted that the proponents of synthetic biology chose to develop their research field under a disciplinary umbrella; they did not try to be part of the NBIC program. This disciplinary choice calls for a bioethics approach to synthetic biology. What kind of ethics is relevant for this emerging technology is in itself a matter of debate.

ethical issues in those more general debates should be taken into account also in the context of responsible development of these nanotechnologies. More directly relevant are the current technical and economic trends in nanomedicine and related discussions on nanobiomedical ethics and on ethical, legal and societal aspects of nanomedicine. This includes nanodiagnostics, nanopharmaceutics, regenerative medicine and the upcoming domain of neuronanoscience. On a more practical level separate policy and stakeholder dialogues are continuing around nanotechnology for agrifood applications and positive and negative potential implications of nanotechnology for animal testing. For each topic, relevant developments in three distinct arenas are addressed. The first summarises recent nanotechnological developments, the second gives an overview of current debates among policy makers and stakeholders at EU level and in some countries, and the third discusses current trends in ethical, philosophical and social science literature. Since nanoscientists, philosophers and social scientists also participate in the policy and stakeholder debates, the issues discussed in the three arenas are overlapping.

This report focuses mainly on particular issues which are emerging in the current debates related to nanobioethics. Because of the diversity of the topics and issues discussed, the report is subdivided in thematic chapters, on Human Enhancement, Synthetic Biology, Nanomedicine, Agrifood and Animal Testing. Each chapter starts with an assessment of current relevant issues raised by nanotechnological and economic trends. These issues are identified in technology sector reports by ObservatoryNano partners. This is followed by an overview highlighting related issues in the current policy and stakeholder debate at EU level and in Member States when identified. Insights from ethical and social science literature examining relevant issues more in depth are added to the assessment. Each chapter concludes by identifying new issues for debate and suggesting who could do what. In a final chapter, the current nanobioethical discussions are placed in a broader context of trends in the debate on ethical, governance and other societal aspects of nanotechnologies.

Human enhancement

Current issues raised by technical and economic trends

The final report of a recent study by STOA, ITAS and the Rathenau Institute on Human Enhancement defined "... 'Human enhancement' as a modification aimed at improving individual human performance and brought about by science-based or technology-based interventions in the human body. This definition includes 'strong', second-stage forms of human enhancement with long-term effective or permanent results as well as 'temporary' enhancements. Because it is not related to a specific definition of health, this is a non-medical concept of human enhancement. Moreover, we distinguish between purely restorative non-enhancing therapies, therapeutic enhancements and non-therapeutic enhancements." (Coenen et al, 2009)

Their report distinguished four types of human enhancements: mood enhancement, cognitive enhancement, bodily enhancement and life expectancy enhancement. A wide variety of technologies could be used for enhancement. However, not all of them make use of nanotechnology. Nanotechnology may be applied to the following medical technologies which could contribute to human enhancement.

- Implants and prosthetics (e.g. pacemaker; cochlear, retina, neuro-implants (such as deep brain stimulation for Parkinson, depression); limb-prosthetics integrated in the nervous system)
- Brain-machine interfaces
- Pre-Implantation Diagnostics (embryo screening)
- Regenerative medicine (organ and tissue replacement)
- Preventive medicine (while not generally considered an enhancement, it could be used to treat healthy individuals, with similar implications as enhancements for society as a whole) (Coenen et al, 2009)

Some current technical and economic trends in Health, Medical and Bio-applications of nanotechnology³ could raise enhancement issues. In particular medical e-textiles for preventive healthcare applications may change definitions of health, broadening the concept from the classical "absence of disease" to more and more dependence on early diagnostics indicating abnormal body functioning long before the person starts to feel ill. This raises ethical issues of enhancement, choices in use of limited healthcare resources and privacy issues. Enhancement issues could furthermore be raised by nanotechnology applied in regenerative medicine. This may in particular contribute to life expectancy enhancement of individuals, as pursued by the Anti-Ageing and Transhumanist movements.⁴

Related areas to regenerative medicine which are also discussed in speculative future scenarios of human enhancement include artificial implants including improvement of pacemakers, cochlear implants, neuro-implants and nanoenhanced surface properties in orthopaedic implants or stents.

Priorities in policy and stakeholder dialogue

Several Parliamentary Technology Assessment institutes (STOA, ITAS, Rathenau Institute), governmental expert groups, NGO's, politicians, journalists and the European Commission have

³ Described in other reports published online by ObservatoryNano, www.observatorynano.org

⁴ <http://www.sens.org/>

addressed Human enhancement and related ethical issues. Discussions revolved not only around potential consequence of nanotechnology or nanomedicine, but also around the consequence of converging technologies (Nano, Bio, Info, Cogno), brain research, ICT implants and as an entirely separate topic.

The report by STOA, ITAS and Rathenau Institute (Coenen et al, 2009) recommended that the European Parliament should install a European body which should develop a normative framework for assessing Human Enhancement Technologies. Until April 2010, the new Parliament has not taken an initiative for such a body, but several new projects have been started:

- A new STOA project on “Making Perfect Life” coordinated by the Rathenau Institute <http://www.rathenau.nl/themas/project/making-perfect-life.html>
- TAB is also still working on the topic of enhancement, in an ongoing TA project <http://www.tab.fzk.de/en/projekt/skizze/enhancement.htm>

In addition, the European Parliament adopted a non-legislative resolution on regulatory aspects of nanomaterials with 362 to 4 and 5 abstentions on 24 April 2009. In this resolution, MEPs stressed the need “to develop stringent ethical guidelines, particularly for nanomedicine, such as ... the limits set on non-therapeutic human enhancement.” (EP, 2009)

In response to the STOA project, the Commission of European Bishops Conferences COMECE published an opinion by the Bioethics Reflection Group on the Perspectives on Human Enhancement by Technological Means (in French). The Group proposes a set of criteria for evaluating human enhancement technologies:

- a) A harmonious development of the person;
- b) Global solidarity including international justice;
- c) Justice in each individual country;
- d) The precautionary principle;
- e) Informed consent and repercussions on future generations;
- f) A case by case evaluation.

In conclusion, the Group took a prudent approach and had strong reservations concerning application of human enhancement technologies in healthy persons, given the potential risks. In any case, a risk-benefit assessment should be made before using such techniques. If the techniques are applied in disabled people, care should be taken to avoid crossing the boundary between therapy and enhancement. The legislator should prevent such technologies from widening inequalities, and instead promote reduction of inequalities. The European Commission should promote particular transparency, especially regarding research projects with an enhancement dimension. The EC should stimulate researchers to actively seek out the dialogue with society and take into account long term implications of their research. The limits of human enhancement technologies should be emphasized: they can't overcome the main problems of human life: suffering, lack of trust and love. For the Bioethics Reflection Group, a humane life requires accepting the limits of the human condition. They call for a fundamental debate on the promise or illusion of the creation of a new human condition. They see the need for a broad debate in the societies on what is desirable for the future of humankind and on the values that should guide the research and development of new technologies. (COMECE, 2009)

The Rathenau Institute published a book on “Life as a Construction Kit,” (Swierstra et al, 2009) exploring ethical and societal issues related to converging technologies (NBIC) for human enhancement and synthetic biology. This book has been offered to the chairman of the Committee for the Dutch National Dialogue on Nanotechnology in September 2009 as a contribution to the debate. In relation to this, the fraction of the SGP in the Second Chamber of the Parliament has asked the minister of Economic Affairs how the public debate on key technologies can be held in an early stage of developments. Minister van der Hoeven replied on 17 December 2009 that this debate can

be held as part of the national dialogue on nanotechnology if participants in this debate choose to table it, current research on ethical, legal and societal aspects of biotechnology by the Centre for Society and Genomics CSG and as part of advice of the Committee on Genetic Modification COGEM. The minister only considered a government induced dialogue meaningful if this can concentrate on concrete, well delineated applications which are expected to emerge in the foreseeable future. She did not consider this to be the case yet, but in light of future developments this assessment may be open to reconsideration. (NL Minister of Economic Affairs, 2009)

In 2007, the UK House of Commons Science and Technology Committee prepared a report on Human Enhancement Technologies in Sports. They recommended that UK Sport should install a committee to examine the ethical issues of doping in sport and advise the World Anti Doping Agency (WADA) on revision of its policy on ethical issues. Both organisations should make funding available for research into ethics of doping and improve their testing regime for use of illegal Human Enhancement Technologies. The UK Government was advised to install a new independent body responsible for testing, investigation and prosecution of doping offences. This organisation should monitor and evaluate new technological developments. The Department for Culture, Media and Sport (DCMS) and UK Sports were recommended to make available funding for research into illegal HETs. On the other hand, the Committee advised to promote use and development of legal Human Enhancement Technologies, and knowledge transfer between relevant disciplines. (UK House of Commons, 2007)

Fritz Allhoff and colleagues (2009) published a document explaining ethical issues in human enhancement to the general public from an American and Australian perspective. Their definition was broader than commonly used in the debate on human enhancement, and includes biological and social aspects like food and education as well as technologies used to assist or enhance the body or mind externally or introduced into the body. Issues raised by crossing the border between the body and the environment were not addressed, because they suggest that there is no such meaningful boundary. Other authors including Daniela Cerqui challenge this way of framing the debate.⁵ Allhof et al considered current ethical issues from a perspective that includes pairings of freedom and autonomy; fairness and equity; societal disruptions; human dignity and the good life; rights and obligations; policy and law. They ended by raising the question whether there is a need for a new ethics.

The Center for Nanotechnology in Society at Arizona State University, USA investigated public attitudes to nanotechnologies and human enhancement among 76 lay people in six groups spread over the USA. Hamlett et al (2008) found that all six groups were concerned about the effectiveness of NBIC regulation and the need for public information and education. Five out of six groups were concerned over the equitable distribution of new enhancement technologies. Therapy was deemed more important than enhancement and stakeholders might play a role in setting the research agenda. Such technologies should be monitored carefully and international safety standards developed. Such technologies should be developed with public and private support to maximise their benefit. According to four out of six groups, ethicists and ethical considerations should be included in decision making on NBIC technologies. Privacy issues and the role of health insurance companies in limiting access to human enhancement technologies were also considered. Half the groups were concerned with terrorist and military use, environmental consequences and implications for civil liberties and free choice. (Hamlett et al, 2008)

Review of relevant ethical and social science literature

⁵ c.f. ObservatoryNano interview with Daniela Cerqui, July 2009, <http://www.observatorynano.eu/project/catalogue/4NB/>

Human enhancement has re-emerged in recent years as a pertinent topic for discussion amongst ethicists and social scientists (Ach & Lüttenberg, 2008; Ryberg, Petersen, & Wolf, 2008; Savulescu & Bostrom, 2008, Guston et al, 2007). This section reports on a number of distinctions and positions relevant to ethical and social discussions about human enhancement.

Logically as well as practically, it is challenging to pinpoint what exactly is meant by human enhancement. The notion of enhancement implies improving humans beyond their normal healthy state. Enhancements may occur with respect to the state of the body and/or mind. Given the fact that often it is very difficult, in some cases even impossible, to define the normal healthy state of the human body and/or mind, human enhancement becomes a somewhat blurry concept. Nevertheless, ethicists and social scientists have done a great deal to differentiate and substantiate the debate about human enhancement.

Typically, enhancement is understood in contrast to therapy. In the medical field, in legislation, and in private insurance contracts, therapy is used as a synonym for treatment meaning the attempted remediation of a health problem, usually following a diagnosis. Enhancement means technological interventions that improve a condition that we might otherwise view as a normal function or a normal capability of humans.

The therapy-enhancement distinction is both simple and practical. It plays an important role in medical insurance coverage decisions, and it may be used as a powerful marker in health policies and legislation. Still, we need to be aware that the distinction does not map easily onto contemporary therapeutic practices. Therapy today includes preventive, supportive or other kinds of therapies, which are treatments to avoid future health problems and to change or otherwise ameliorate the patient's comfort, looks, life expectancy, well-being etc. One may think of plastic surgery, contraceptive medicine, palliative care, cosmetic dental procedures, and much else. These are all technological interventions aimed at improving or enhancing human capacities in a normal or near-normal state of being.

A number of objections has been raised against using the therapy-enhancement distinction in ethical reflections on enhancement (Bostrom & Roache, 2008; Daniels, 2000). The distinction begs the question of defining a normal healthy state. One may consider human nature from the species-typical level or from the statistically-normal range of functioning of individuals or from historical, philosophical or religious points of view. We settle for the observation that there is no consensus on the ethical question of making out a natural human baseline according to which we may distinguish between moral and immoral human enhancements (Daniels, 2000).

The therapy-enhancement distinction has already been used in a defensive sense (therapy good, enhancement bad) as a powerful legitimacy argument in the gene therapy debate. Leach Scully and Rehmann-Sutter argued that this use of the therapy-enhancement distinction has discriminatory social side effects, because it relies on a normalization of the human body with negative implications for those with disabilities or with better-than-average capabilities. (Leach Scully & Rehmann-Sutter, 2001)

Notwithstanding the fact that the therapy-enhancement distinction is difficult and that the nature of the human being is notoriously hard to define, Johann S. Ach has summed up various objections against the idea of improving or transforming human performance (Ach, 2008). These include:

- Risks and undesirable effects: Assessing the risks and undesirable effects is not a problem specific to human enhancement. However, as enhancement interventions generally are not directed towards curing illnesses, risks potentially are of high relevance.
- Reducing our sense of individuality, responsibility, and human agency: In Western cultures, a person's achievements and actions normally are attributed to the person as individual and responsible human agent. If the performance of a person no longer can be seen as the self-

revealing doing of a genuine “doer”, human enhancement may end up reducing the individual’s human agency in terms of intelligibility and responsibility (see also: (The President's Council on Bioethics, 2003).

- Social injustices: Since enhancement interventions may be expected to become quite costly, it seems to be justified to worry that human enhancement technologies will amplify social inequalities on national and international levels. Despite the fact that it may prove impossible to sort between proper and improper motives, it still remains an ethical question to ask which aims are served by investments in the development of human enhancement technologies (see also: Siep, 2008).
- Competition spirals: Since the application of human enhancements technologies is in many cases motivated by the desire to gain competitive advantages (whether on behalf of other individuals or other organisations), the ability to stay ahead of other “enhanced” actors would depend on ever more effective enhancement measures. The standards, according to which human performances would be judged, will then become all the time more fluent and flexible.
- Degradation of social norms and values: If human standards become increasingly moving targets, the perpetuation of dubious norms and values would become more likely. The spread of enhancement technologies among a meritocracy might entail exaggerated and possible morally questionable social demands leading to a degradation of accepted social norms and values.

Rather than attempting to envision the possible misuses of human enhancement as such, Donald Bruce (2007), reporting on an expert working group on converging technologies for human functional enhancement under the auspices of the NanoBio-Raise project, proposes instead to speak about incremental vs. radical enhancements, see table 1.

Incremental enhancements	Radical enhancements
...represent a change of degree in the enhancements of humans capacities or in technological innovations	...envision a change of state regarding existing human capacities and conditions or regarding the very purpose of technology
...involve technologies which are external to the body and which add to it	...uses (nano)biotechnologies within the body/brain
..can be either irreversible or reversible	...introduce permanent and irreversible changes
...generally assume the above-mentioned distinction between the therapeutic and enhancement interventions	...are employed to transform human capabilities and as such go beyond therapeutic contexts

Table 1 Relevant parameters for distinguishing between incremental and radical enhancements. Adapted from (Bruce, 2007).

Incremental enhancements include types of technological interventions that strengthen or increase human capabilities within biological limits. For example, we use optical lenses enabling us to see more clearly, to see further, or to see objects at the microscopic scale. This is an external and fully reversible enhancement of human vision. Also, it is quite unproblematic to make a distinction between therapeutic and non-therapeutic uses of optical devices. When we move to radical enhancements, however, we enter the field of envisioning completely novel human capacities. Staying with the example of human vision, we could think about technological means of using the eye as an interface between human consciousness and computer-based information systems. Radical enhancement often includes ideas about human transformation or even transcendence such as those propagated by transhumanist thinkers (Bostrom, 2006). The expert working group sought to take such claims seriously, while at the same time warning against focussing on the ethical and social consequences of technological improbabilities.

Similarly, Toumey identified transhumanism and cyberimmortality as dominating ideas in debates about nanotechnology and ethics, arguing that such issues tend to make religious writers and others “systematically hostile to a very broad technology” (Toumey, 2008). He concludes:

“This [the dominance of transhumanism and cyberimmortality in debates about nanotechnology] is both a strategic blunder and a regrettable approach to knowledge. Nanotechnology in the present, the near-future, and indeed the far-future is much more interesting than the question of enhancement and immortality alone”. (Toumey, 2008)

Along the same lines, Khushf suggested a midterm horizon for addressing ethical issues integral to nanotechnology (Khushf, 2007a). Like Toumey, Khushf saw the far-term time horizon as unsuitable for addressing ethical issues integral to nanobiotechnology, such as human enhancement, since debates then tend to become speculative and uninformed by existing technological trajectories. Khushf also maintained that the narrow focus on near-term, science-based, results-oriented topics will result in missing many important ethical problems. Pleading for a mid-term time horizon for nanotechnology ethics, Khushf argued that enabling this kind of ethical reflection as a minimum requires bridging the gap between the professional research cultures of science and engineering, on the one hand, and the humanities, law, and policy, on the other.

Bruce (2007) discussed implications of converging technologies for human functional enhancement, in particular brain chips, chemical stimulants and electrode stimulation of the brain. None of these cases promises benefits for society as a whole that warrant public funding for the technology development. The implications of these enhancement technologies are likely to affect not only the users but society as a whole. Social issues related to human enhancement warrant further study of governance and legal aspects, as well as public awareness raising activities. Bruce (2006) also explored ethical issues of nanomedicine, in particular implications for human nature. Furthermore, the relationship between human enhancement and perfectionism has been examined by Catharine Larrère (2008).

A key concept in the discussion is “human health”. There is no consensus on what this means. Gregor Wolbring has examined the different concepts of health which play a role in the current debate on enhancement. These range from simply “the absence of illness” via “a state of full physical, psychological and social well-being” according to the World Health Organisation, to improving capacities over biological species boundaries. (Wolbring, 2005)

Related to this, there is disagreement on the concept of disability. In a discussion paper published by the World Council of Churches, five models of disability were distinguished:

- The medical model of “disability / impairment”
- The medical model / social determinants / social well-being combination model of “disability / impairment”
- The medical model / transhumanist / enhancement determinants / social well-being combination model of “disability / impairment”
- The pure transhumanist model of “disability / impairment”
- The social model of disability. (Lee & Robra, 2005)

In the philosophical and ethical literature related to nanobioethics, some relatively new elements have recently entered the debate. The first is a broadening of the discussion on what it means to be human away from definitions of “human nature” towards alternative broader concepts including the European approach to Converging Technologies for the European Knowledge Society (Ferrari, 2008), “human sustainability” (e.g. van Est et al, 2008) and “human flourishing” (e.g. Sandler, 2008). Similarly, Hassoun (2008) finds that some nanotechnology based human enhancement may be impermissible because of two environmental ethics arguments: our species has aesthetic value and it plays valuable ecological roles. Both aspects may be threatened by nanotechnology-enabled human

enhancement. The other new element in the debate on human enhancement is increased interest in religious views on the issues, incorporating western as well as non-western perspectives. (Belt, 2009; Hongladarom, 2009)

Conclusions

To conclude, there is a current political and stakeholder debate on human enhancement at EU level and in several countries. Especially in the area of Human Enhancement Technologies in Sports, there are initiatives to install Parliamentary bodies for monitoring the developments and governing the developments. Nanotechnology may be applied in some human enhancement technologies, including preventive healthcare and regenerative medicine. Current issues in the philosophical and ethical debate include risks, implications for human self-perception and concepts like health and disability, social injustices, competition spiral and degradation of social norms and values. Incremental and radical enhancements are distinguished, and several authors recommend focusing the debate on short to medium term developments rather than very futuristic scenarios. New issues for debate include different concepts for discussing the human condition and religious viewpoints on human enhancement. Several parliamentary Technology Assessment organisations and philosophers and social scientists are already discussing human enhancement, but this debate is moving away from technological developments to trends in new uses of existing (medical) technologies for enhancement rather than therapy.

Synthetic biology

Current issues raised by technical and economic trends

The European Group on Ethics gave the following definition: Synthetic biology includes the design of minimal cells/organisms (including minimal genomes); the identification and use of biological 'parts' (toolkit); and the construction of totally or partially artificial biological systems. (EGE, 2009) Some parts of nanobiotechnology can be considered to be included in this definition. Even though nanotechnology is not the main focus of the debate, some of the arguments are also relevant to current trends in nanobiotechnology. These relevant concerns include paradigm changes in biology, worker safety, governance and moral and ethical boundaries.

The current policy and stakeholder debate on ethical aspects of synthetic biology is mainly related to DNA and other biotechnological materials and trends in biology. Synthetic biology parts and devices are often nano-scaled objects. Some novel nanobiostructures considered to be nanomaterials may contribute to the development of synthetic biology. These include synthetic cells e.g. for drug discovery: elements, liposomes, polymers, nanoemulsions, novel fabrication techniques and nanomaterials to create cell like structures, synthetic membranes. (ObservatoryNano, 2009, Whitthall, 2009)

A recent example of interdisciplinary research combining nanotechnology with Synthetic Biology is the experiment in which viruses were genetically modified to attach to Single Wall Nanotubes (SWNT) on one side and amorphous iron phosphate on the other, thereby acting as scaffold for assembling nanostructured Lithium Ion battery electrodes. (Yun Jung Lee, Hyunjung Yi et al, 2009) EU-funded projects combining nanotechnology and synthetic biology include BIONANO-SWITCH (2006-2010), where a biological nanoactuator is designed and applied as a molecular switch for biosensing in a lab on a chip. (NEST-2005-PATH-SYN) Another relevant project is NANOMOT,

developing synthetic biomimetic nanoengines: a modular platform for engineering of nanomechanical actuator building blocks (2006-2009).⁶ The GOLEM project aims to understand and investigate the use of bio-inspired bonds to self-assemble small components. (2006-2010)⁷

These and other projects on the boundary between nanotechnology and synthetic biology illustrate the need to take into account issues in the policy and stakeholder debates as well as those identified in ethical and social science literature on synthetic biology also in governance of nanobiotechnology. Some of the outcomes of the broader debate are also valid for research in nanobiotechnology.

Priorities in policy and stakeholder dialogue

In recent years, the European Group on Ethics (EGE, 2009) and other policy related organisations including the Rathenau Institute (Netherlands) (Vriend, 2006), the Nuffield Council for Bioethics (UK) and the Woodrow Wilson International Center for Scholars (USA) have examined potential ethical and societal issues related to synthetic biology.

Paradigm changes

The Rathenau Institute (Netherlands) foresaw a number of paradigm changes from genetic modification to synthetic biology. One of these is relevant for nanobiotechnology: From adaptation or modification of existing biological systems to design and construction or modulation of new biological systems. Synthetic Biology is considered to be “a new emerging scientific field where ICT, biotechnology and nanotechnology meet and strengthen each other”. (Vriend, 2006) The explicit contribution of nanotechnology is limited to visions of nanomachines as originally outlined by Feynman (1959) and Drexler (1986), which is however not generally considered mainstream nanotechnology research. The bio-nanotechnology contributions to synthetic biology are labelled biochemistry. Novel nanobiostructures may contribute to a paradigm shift towards a so-called biobased economy: nature as a starting point for human progress instead of nature as the vulnerable border. (Walhout, 2009) The European Group on Ethics also expected that “synthetic biology could lead in the future to a paradigm shift in understanding concepts of life.” (EGE, 2009)

Governance

The European Group on Ethics (2009) asked The European Commission to develop a code of conduct for synthetic biology similar to the one it developed for nanotechnology and to survey possible gaps in risk assessment and regulations for synthetic biology. For instance, to deal with biosecurity implications, the Biological and Toxin Weapons Convention (BTWC) should incorporate provisions on the limitation or prohibition of research in synthetic biology. (EGE, 2009, Walhout, 2009, Balmer & Martin, 2007) In general, codes of conduct for biosecurity exist already as instruments for self-regulation of the life science community in accordance with provisions of the BTWC.⁸

Governance, Intellectual Property Rights (IPR), trade and global justice issues should also be addressed by the EU. A debate should be started on which synthetic biology inventions can be patented and which not. The European Group on Ethics (EGE) has the authority to assess the ethical implication related to patenting, according to article 7 of the EU Patent Directive 98/44/EC. They called upon the European and national patent offices to “refer contentious ethical issues of a general relevance to the EGE for consideration. This is particularly important if a class of inventions that ought not to be directly exploited commercially has to be defined”. (EGE, 2009, Walhout, 2009,

⁶ <http://cordis.europa.eu/fp6/nest.htm>

⁷ <http://www.golem-project.eu/>

⁸ e.g. <http://www.knaw.nl/publicaties/pdf/20071092.pdf>

Balmer & Martin, 2007) In particular, private research gives rise to Intellectual Property Rights issues. An example of this is Craig Venter's work and his search for novel organisms or functions in international waters.⁹

Ethical issues related to synthetic biology should also be taken into account in international dialogue on trade related issues. The same biosafety and biosecurity precautions should govern products imported into the EU as domestically produced products based on synthetic biology. The EU should invest in international research cooperation to overcome the technology gap with developing countries in synthetic biology. (EGE, 2009)

The respondents in a public opinion survey on synthetic biology in the USA called for an independent oversight structure to advise the (US) federal government and were concerned who would set moral and ethical boundaries. (Pauwels, 2009)

Moral boundaries

Participants in a focus group on synthetic biology in the USA were concerned about conflicts between religion and science (Playing God), and opposed introducing anything synthetic into one's own body. These issues also relate to nanotechnology. (Pauwels, 2009)

The European Group on Ethics (EGE) proposed that research in synthetic biology must respect basic human rights and human dignity, but also safety, sustainability, justice, precaution, freedom of research and proportionality. (EGE, 2009)

Public dialogue

The European Group on Ethics (EGE) asked the EU and member states to promote public dialogue. Because the EGE expects that "synthetic biology could lead in the future to a paradigm shift in understanding concepts of life; it therefore calls on the Commission to initiate an open intercultural forum to address the issues, to include philosophical and religious input." (EGE, 2009)

Support for research

The European Group on Ethics (EGE) recommended that basic and applied research in synthetic biology and in ethical and societal aspects of synthetic biology such as risk assessment and safety; security issues of synthetic biology; ethical, legal and social implications; governance; and science and society (including media and the public) should be supported by the EU and its member states. (EGE, 2009)

Worker safety

In nanobiotechnology research projects, biological materials are commonly handled by a multidisciplinary workforce. This is risky, because someone trained as a physicist or chemist may not be aware of common safety and security measures for handling biological materials and vice versa. A related discussion is on the increasing trend that amateur scientists engage in synthetic biology research in their garage and the potential biosecurity and biosafety risks this entails. (Whitthall, 2009) Maria Powell & Mathilde Colin compiled lists of internet resources on nanotechnology and occupational health and safety¹⁰. Most of the discussion is about occupational safety of engineered (non-biological) nanomaterials, not about risks caused by a lack of adequate training of multidisciplinary workers in handling biological materials.

⁹ http://fora.tv/2008/02/25/Joining_3_5_Billion_Years_of_Microbial_Invention

¹⁰ <http://www.nanoceo.net/nanorisks>

Review of relevant ethical and social science literature

In a recent analysis of the debate on synthetic biology, Henk van den Belt (2009) found that “Playing God” was more used as an argument by secular stakeholders like the Canadian NGO ETC Group¹¹ and by journalists than by theologians and bioethicists. Van den Belt noted that the current debate on the meaning of life is held from an anthropocentric perspective and that transgressing the boundary of the human being is also the main issue at stake in synthetic biology. (Belt, 2009)

Deplazes, Ganguli-Mitra and Biller-Adorno (2009) outlined an agenda for the ethics of synthetic biology including method, application and distribution related issues. Whereas many of the ethical issues raised by synthetic biology are not new, they consider it necessary to discuss them again because the context of the issues is different from before, and because reflection about the issues is a worthy goal in itself. Synthetic biology also raises new ethical issues, but these new issues are probably not related to novel nanobiostructures.

In the same volume, Alexander Kelle discussed a new governance framework for addressing biosecurity implications of synthetic biology as well as other life sciences, and Markus Schmidt discussed biosafety aspects, especially those related to “democratising life sciences”, in the sense that amateur scientists may also acquire the tools to engineer biology and cause harm to themselves, their neighbourhood and the environment. Kenneth Oye and Rachel Wellhausen proposed a new evaluative framework to assess intellectual property issues for new technologies including synthetic biology. The framework has two axes: private ownership versus commons and clarity versus ambiguity. (Schmidt et al, 2009)

Earlier, social scientists and ethicists have discussed analogies between visions of nanoscience and converging technologies and historic visions of homunculus, golem and Frankenstein. Bernadette Bensaude-Vincent considered nanotechnology to revitalise the chemist’s ambition to answer the big questions about life and the universe and biomimetic chemistry to be part of a long tradition in chemistry to challenge nature through the artificial creation of life. (Bensaude-Vincent, 2007) Jean-Pierre Dupuy reflected on philosophical discussions of stories in which artificial life was created including the creation of the golem by Jeremiah. This application of human knowledge to fabricating a living being was considered good, because we have to test our knowledge. But once created, the golem protested because his existence would lead to uncertainty whether a living person encountered was created by God or by Jeremiah. At his request, Jeremiah destroyed the golem again and concluded “we should not renounce attaining the perfect knowledge that makes us capable of creating a man, but once we attain the knowledge, we should abstain from acting on it.” Dupuy, citing Atlan recommends to reflect on this lesson. (Dupuy, 2007)

Conclusions

Even though most issues in the current debate on synthetic biology are not related to nanotechnology, some trends in nanobiotechnology may also be affected by the policy measures suggested by the European Group on Ethics and others. Progress in novel nanobiostructures and the public and philosophical debates on synthetic biology do not give rise to completely new issues for debate. However, some issues which are not really new may require more attention of policy makers. The safety of workers in multidisciplinary research labs and of amateur scientists is such an issue which requires constant attention. Governance of intellectual property of new technologies including nanobiotechnology could also benefit from new ideas proposed by the European Group on Ethics and other experts. The EU Code of Conduct for Nanotechnology Research (2008) could serve as an example for a code of conduct for synthetic biology as proposed by EGE. It might be useful to

¹¹ www.etcgroup.org

take into account the outcome of the current evaluation of the implementation of the nanotechnology code in the Nanocode project¹². Philosophers reflecting on attempts at creating artificial life place nanotechnology and synthetic biology in a century old tradition in natural sciences to mimic or improve nature. They raise ethical questions like: should everything that scientists are capable of, be allowed?

Nanomedicine

Current issues raised by technical and economic trends

Nanomedicine is a broad concept which can be defined in different ways. A definition which influences European nanomedicine research was given by the European Technology Platform (ETP) Nanomedicine: “Nanomedicine exploits the improved and often novel physical, chemical and biological properties of materials at the nanometre scale. Nanomedicine has the potential to enable early detection and prevention, and to essentially improve diagnosis, treatment and follow-up of diseases.” This ETP distinguishes three subareas in their current Strategic Research Agenda: nanodiagnostics, nanopharmaceutics and regenerative medicine. In the future, a fourth area of neuronanoscience may be added.¹³ NanoBioRaise made a clear distinction between nanomedicine and medical applications of nanotechnology. “Nanomedicine is based on molecular knowledge of the human body and it involves molecular tools for the diagnosis and treatment of disease. Medical nanotechnologies are more general: these concern public health monitoring, the integration of medical practices into daily patterns of work and leisure, the redefinition of the physiological body as a body of data, and the reorganisation of the therapeutic context with its medical experts, insurance companies, state interests, and healthcare institutions.”¹⁴ In this report the discussion will be mainly limited to nanomedicine.

In diagnostics, nanotechnology already plays a crucial role, in *in vivo* imaging and *in vitro* diagnostics. In the future, nanotechnology may help improve current and future imaging systems, design new contrast agents, improve *in vitro* diagnosis in general and enable point-of-care applications. (ETP Nanomedicine, 2009) A number of ethical issues related to applications of diagnostics and their implications for patients, doctors and the healthcare system in general are already widely debated. These are not limited to nano-enabled diagnostics. The aim of nanodiagnostics is to detect single defective cells or biomarkers predicting the onset or initiation of disease. Such early diagnosis is controversial because on the one hand it may enable earlier and less costly and burdensome treatment of patients before symptoms manifest themselves. On the other hand, they may lead to treating healthy persons who might not have become ill during their lifetime or induce anxiety among the population about their health. In theranostics a drug is encapsulated in a drug delivery vehicle incorporating diagnostic functionality. This could be designed in such a way that the theranostic once injected in the bloodstream can identify diseased tissue and automatically start treatment without human intervention. This has already given rise to public and ethical concerns about the lack of human intervention in the therapy.

In nanopharmaceutics, nanotechnology is already important, and progress is expected in miniaturising micro-drug delivery, activatable nanomedicines using external non-invasive forces and nano-enabled devices for drug delivery. (ETP Nanomedicine, 2009) The current debate focuses on IPR

¹² <http://www.nanocode.eu/>

¹³ Source: website ETP-Nanomedicine, <http://www.etp-nanomedicine.eu/public>

¹⁴ www.nanobio-raise.org

(Intellectual property rights) issues. The key issue is patent extension as encapsulation of existing therapeutics allows pharmaceutical companies to extend the patent life of these drugs by another 15 years. (Alavijeh, 2010) This has implications for the market positions of generic drug manufacturing companies. It may also mean that the price of one dose of the encapsulated drug is higher than of one dose of the non-encapsulated drug. However, if the nanodrug delivery vehicle is used to encapsulate chemotherapy, for instance for cancer treatment, the costs of the whole treatment of a patient and the side effects for the patient may be much lower than conventional chemotherapy. In balancing costs and benefits, all these effects are relevant.

Regenerative medicine is in an earlier stage of development and it is very important to establish a sound regulatory framework in this area and ensure the translatability of research results into products. Nanotechnologies could enable smart bio-materials for improving medical instruments or facilitate regeneration of damaged tissue by themselves. Nanotechnologies could furthermore enable production and transplantation of cells for cell therapy. Commercialisation of stem cells can be enabled by the identification of existing cell differentiation agents using novel (nano)technologies. (ETP Nanomedicine, 2009)

In a recent bibliometric study of the emerging field of regenerative medicine, Peter van den Besselaar and Thomas Gurney (2009) have found that regenerative medicine related advanced materials papers were not published in nanoscience journals in 2003, but that they were published there in 2007. Regenerative medicine is a broader area of research, where nanotechnology is being applied only recently.

An example of nanotechnology enabled regenerative medicine applies a designed self-assembling peptide nanofibres scaffold to recover brain function, in particular reversal of blindness. Another self-assembling peptide can be used to stop bleeding anywhere in the body within 15 seconds. (Ellis-Behnke, 2010)

General dynamics in the field of regenerative medicine have been mapped in a study on Converging Technologies published by the Dutch Study Centre for Technology Trends (STT). Tissue Engineering was a promising research area in the 1990s, but interest in it declined because it could not meet the high expectations. More recently, tissue regeneration has gained interest after promising developments in genomics, proteomics, stem cell research and biomaterials. Potential applications include cell therapy as remedy for heart failure and growth factors for orthopaedic surgery of the spine. The chances of success of regenerative medicine are influenced by a wide variety of factors including cost effectiveness, insurability, regulation and normative issues. The development is a contingent process which is hard to predict, but it is necessary to reflect continuously in a step-by-step learning approach on possible trajectories so that society can be better prepared for the new technological possibilities. (Doorn, 2006)

Priorities in policy and stakeholder dialogue

In 2009, the policy and stakeholder dialogue on European level has been concentrated in the EU funded NanoMed Roundtable and in EuroNanoBio. The NanoMed Roundtable included working groups on economic, regulatory, ethical and social issues, patients' needs and public communication. Patients needs include access to reliable sources of balanced information on nanomedicine. The future research agenda on ethical and societal aspects of the NanoMed Roundtable includes developing better definitions of nanomedicine research and its aims and programme based on philosophical and social analysis. Philosophers and social scientists should take into account the feasibility of applications of nanomedicine in their deliberations, as well as promises, hopes and anxieties. Global governance of nanomedicine aimed at fair and sustainable benefit sharing should include low income countries. There is a need for reliable data to predict the impact of nanomedicine on healthcare costs and benefits and market growth. The European Commission DG Health &

Consumer Protection (SANCO) and national regulatory bodies should coordinate development of a proactive regulatory system for nanomedicine. (NanoMed Roundtable, 2010) EuroNanoBio proposed elements of a roadmap for nanobiotechnology in Europe in the form of a European network of regional clusters. This network should not only cover scientific and economic aspects, but also education and ethical, legal and societal aspects. Cooperation with non-European actors should be included. (EuroNanoBio, 2010)

In the USA, the Center for Nanotechnology in Society also organised an expert scenario development workshop on nanodiagnosics (Doc-in-the Box). This was considered to contribute to more responsive, socially robust decision making on the technology development. Concerns addressed in the workshop include: access to and ownership of the technology; first applications and path dependence; design characteristics; and technical aspects like reliability, targeted to infectious or chronic diseases. (Selin, 2008)

Review of relevant ethical and social science literature

Nanomedicine plays a prominent and promising role among emerging nanobiotechnologies. There is a wide range of materials and potential applications encompassing sensors for single-molecule detection, identification of biomarkers, nanoparticles and nanocarriers for the detection and imaging of cancers, and the delivery of therapeutic molecules. In contrast to (radical) human enhancement technologies, nanomedicine is a reality in both medical research and clinical practice, offering new and promising approaches to fundamental problems in medicine (Ferrari, Philibert, & Sanhai, 2009).

As in the case of using nanobiotechnologies for human enhancement, it has been considered fruitful for ethical debates to make a distinction between two kinds of nanomedicine (Khushf, 2007a,b). Type-1 nanomedicine is incremental developments that are continuous with existing therapies and ongoing, non-nano-related clinical research activities. This type of nanomedicine is being developed to solve conventional medical problems of a very specific kind. The ethical problems therefore need to be articulated in close relation to the specific issues of clinical interest. Unfortunately, no rigorous, systematic review of such issues exists. Type-2 nanomedicine, in contrast, is the more foundational, transformative kind of nanomedicine, which often is closely linked to broader and more radical visions of emerging nanotechnologies. In these visions, nanomedicine becomes simply the application of a comprehensive and fundamental understanding of biology's nanosystems, including diseases and cures. Ethical reflections relating to type-2 nanomedicine requires thinking critically as well as sympathetically about such visions and their social and ethical implications. It includes ethical issues related to interdisciplinary research; IPR and publications; informed consent and confidentiality; doctor-patient relations and personalised medicine; reductionist models of nanomedicine and enhancement. (Khushf 2007a)

With a special emphasis on applications of nanomedicine in early diagnosis of cancerous tissues, Ferrari et al. (2009) proposed using the four cardinal principles of Childress and Beauchamp: beneficence (the utilitarian perspective of maximizing community benefit), non-maleficence (the Hippocratic mandate of "First, do no harm"), respect (including autonomy, or the patient's right to decide), and justice (including fair access to health care). Recognizing that nanomedicine promises extraordinary opportunities for medical advances within cancer research and, in particular, offers hope for early detection of cancer and individualized therapies, the authors proposed that nanotechnology-enabled personalized medicine poses ethical questions of autonomy and privacy. Moreover, like other emerging nanotechnologies, nanomedicine might become available only to privileged societies or parts thereof. Such questions cannot be addressed only by small groups of nanotechnologists and/or nanoethicists but need to be discussed in the broadest community context possible.

There are a number of possible applications of nanomedicine, most of which could have a potentially huge impact on society: improvements of patients' quality of life, reduction of societal and economic costs associated with health care, early detection of pathological conditions, reductions in the severity of therapies, and improved clinical outcomes for patients. The market for drug delivery technologies and biomaterials is expected to grow significantly in the coming years. Government agencies have already invested huge amounts in developing nanomedicines, while, at the same time, several national and international working groups have been looking into the promises and risks of such developments. Analyzing six reports on the topic of potential harm and benefits of nanomedicine, Lenk and Biller-Andorno (2006) identified four areas of emerging ethical issues.

- (1) *Risk assessment in medical research, diagnosis and therapy.* Two problems appear as particularly relevant to risk assessments of nanomedicine. First, there are questions of toxicity and how to prevent significant health complications of patients and test persons during clinical trials. Second, there is the issue of whether or not we could expect a combination of risks in consequence of the combination of nanobiotechnologies, relevant first and foremost for nanobiotechnologies used in gene therapy.
- (2) *Questions of personal and human identity.* Nanobiotechnology comes closer and closer to bodily functions and mechanisms at the atomic and molecular level, raising doubts and questions about the genuinely human qualities of mind and body. Ethical distinctions between humans and non-humans become more pertinent. For example, similar to applications such as xenotransplantation, it could be expected that patients would react to receiving new functional molecules or even virus-like agents in their body. Nanotechnological innovations in medicine could also be used to increase human life expectancy, thus not only having a socio-economic impact on our society's age structure but also changing our self-understanding of the normal human life.
- (3) *Enhancement by possible nanotechnological implants.* The issue of transcending or transforming human identity has already been dealt with in the section about human enhancement. We should be aware that most implants for fulfilling aesthetic, athletic, sexual, cultural, and work-related goals are propagated and justified by the potential users themselves, even when others consider such interventions very risky or even unethical.
- (4) *Distribution of risks and potential benefits.* As mentioned above, the development and application of new nanomedicine products raises questions about distributive justice. In an important paper, Mnyusiwalla et al. (2003) suggested that such questions arise especially in the context of emerging technologies. They also argued that nanotechnologies could be used to promote distributive justice by making better prevention, diagnosis and treatment available to underdeveloped countries.

In addition, Slade (forthcoming) made the point that human subjects in clinical trials are important population to consider from an ethical perspective -- especially with respect to intentions of reducing health disparities between racial groups, as racial minorities participate much less in clinical trials. Lenk and Biller-Andorno (2006) emphasize that these issues have all been raised before in the context of biotechnology. Their view is supported by other authors (Bawa & Johnson, 2007; Brownsword, 2008, 2009; Ebbesen & Jensen, 2006). Other authors such as Haker (2008) suggest that due to the uniqueness of nanobiotechnologies, allowing manipulations of fundamental properties and functions at the basic level of organisms, it would be hastily and perhaps naive to simply assume that nanobiotechnology will not have ethical implications of a new quality, too. Haker suggests that we need to further develop the ethical instruments of analysis and scrutinize them in the actual evaluation of nanomedicine, before we can draw the conclusion that there is nothing new under the sun.

Notwithstanding the disagreement among ethicists about the novelty of the ethical implications of nanomedicine, we might see new and controversial issues emerging in public debates about nanomedicine. Lenk and Biller-Andorno (2006) observe that there are huge differences in public responses toward particular technologies. Whereas some technologies are readily accepted, others

such as gene therapy become the object of long-lasting and bitter debates. Consequently, it is not prudent to think about public opinion on nanomedicine simply as lacking in scientifically and ethically relevant information. They conclude:

“So even if the ethical arguments are not new or unique to nanomedicine and may have been rehearsed before in the context of other technologies, spelling them out again and giving society the opportunity to weigh them is important in order to foster as fair, rational and participatory debate as possible, which can then serve as a basis for well-informed, responsible societal and political decisions. Factual, balanced reports by advisory or expert bodies can play an important role in that regard, particularly when they include an interactive element such as public hearings or open work group sessions”. (Lenk & Biller-Andorno, 2006, p. 182)

One aspect which appears to be specific to the use of nanotechnologies in biomedicine is the potential need for rethinking the traditional model of the patient-physician relationship (Jotterand, 2007). According to the traditional model, there is an imbalance of expertise and power between the sick and the medical professional. This means that the patient depends on the physician for knowledge and possibly assurance, and that the relationship builds on mutual trust, technical competence, and moral integrity. With the advent of smart medical devices such as nanosensors, the patient will be empowered to monitor and possibly pre-diagnose their own condition. Patient might also be able to make own decisions with respect to medical treatment because new innovative technologies could make it easier to implement low-risk cures. Such developments will tend to reinforce the emergence of more knowledgeable patients, thus making more symmetrical the knowledge/power relationship between patients and physicians. Moreover, personal trust between patients and physicians will be more difficult to establish as diagnostic expertise is becoming embedded in devices, not in personal relationships. Moreover, if the diagnosis of physicians is different from the results of the diagnostic nanodevices, such devices might even tend to break down the relationship of trust that is crucial to the practice of medicine as we know it. Brigitte Nerlich reported the case of a woman who is diabetic and wanted to use an insulin home testing kit. Her doctor did not allow it.¹⁵

Berger et al (2008) wanted to raise awareness among nanoscientists about ethical, legal and social aspects (ELSA) of brain implants improved with nanotechnology. Relevant issues include short term testing and clinical trials in the existing regulatory framework, short and medium term risk aspects and long term enhancement issues. These issues should be addressed by including ELSA experts and regulatory bodies from an early stage in the research. Bawa & Johnson (2007) found some issues to be discussed differently due to the interdisciplinary nature of nanotechnology: privacy, confidentiality, risks and benefits, defining diseases and enhancement. Resnik & Tinkle (2007) warned that clinical trial with nanomedicine raised more urgent (though not really novel) risk minimization, management and communication issues. Nerlich, Clarke & Ulph (2007) found that risk perception by young adults of therapeutical interventions was influenced more by differences between a single or multiple doses than by differences between ordinary drug and nanodelivery. Resnik & Tinkle (2007a) expected that significant health risks of nanomedicine can occur in phase II and III clinical tests, and foresaw increasingly important issues of social justice, access to healthcare and physical enhancement. Lupton (2007) foresaw that nanomedicine would enable repair of the human body from the inside out, and explored the role of law, ethics and suitable control mechanisms for governing nanomedicine.

Besselaar and Gurney analysed the philosophical ethical literature on regenerative medicine and concluded that the debate on these issues is only just beginning. Stem cells are most discussed. The

¹⁵ Nerlich, Brigitte, personal communication, March 2010

issues identified in 124 selected papers include: ethical issues around embryonic stem cells, cloning and cell transplantation; legal and political aspects of stem cell research and therapy; and the public debate about stem cells. Other issues include: genetic diagnoses, issues around commercialisation, medical technology in developing countries such as China and India and cord blood banking. (Besselaar & Gurney, 2009)

Conclusions

The debate on nanobioethics and ELSA issues related to nanomedicine is a continuation of earlier biomedical ethics debates. Some experts referred to in this chapter don't see any new issues, whereas others have a hard time pinpointing what they consider new. Technical and economic developments in nanomedicine do suggest that it is important for the scientists and industrialists engaged in developing nanomedicine and the philosophers and social scientists studying their consequences to maintain close working relations. For instance the discussion on Intellectual Property Rights issues and balancing the rights of innovators and access to care should not be limited to the costs of one dose of a patented drug compared to one dose of a generic drug, but take into account the costs of complete treatments with drugs encapsulated in nanodrug delivery and non-encapsulated drugs for the healthcare system and for the patient. Another still unresolved issue is the possibility that medical service companies use personal biological data for profit making purposes.

Current issues discussed in ethical and social science literature which should be discussed in broader forums include autonomy and privacy issues related to personalised medicine and access to nanomedicine for deprived populations. In general, there are six areas of relevant ethical issues, including risk assessment in medical research, diagnosis and therapy, questions of personal and human identity, enhancement by possible nanotechnological implants, distribution of risks and potential benefits, which groups are included in clinical trials, and the potential need for rethinking the traditional model of the patient-physician relationship.

Philosophers see the need to engage with embedded notions of health, disease, molecular medicine etc and with the normativity of these concepts.

Nanotechnology in agrifood

Current issues raised by technical and economic trends

Nanotechnology can be applied in agriculture as well as in food and food production. According to the ObservatoryNano report on nanotechnology in agriculture, nanotechnology in the agricultural sector is developed in a changing societal, economic and environmental context, for which nanotechnology is expected to contribute to solutions. These include:

- Inflation of food prices,
- An increasing world population shifting their diet from vegetarian to meat and fish,
- Climate change,
- Adaptive supply chains from farm to fork,
- Environmental sustainability.

Nanotechnology is expected to contribute to technological innovation of pesticides and nutrients to address some of the demands caused by these changing circumstances including increased efficacy, controlled release and targeted delivery for agrochemicals and other forms of fertilisers, nutrients, plant growth enhancers or inhibitors, fungicides, herbicides and pesticides. (Robinson et al, 2010)

Applications of nanotechnology in food and food production include food packaging, food ingredients and food processing technologies. Novel foods and diagnostics based on nanotechnology may also play a role in preventive healthcare, because they enable the adaptation of the diet of a person to the actual needs of the body for specific nutrients.

Priorities in policy and stakeholder dialogue

The policy and stakeholder dialogue on nanotechnology in agrifood is not unequivocally positive. The current debates discussed below can be subdivided according to the sector in which nanotechnology is applied: agriculture and food processing. Other debates are related to the application of nanotechnology: in novel foods or as food ingredients. Regarding progress in agricultural technologies, the European Group on Ethics sees potential benefits as well as risks. There is a controversy around the use of nanoencapsulation and targeted delivery of pesticides and the possible risks for ecosystem health and non-target organisms. Related to food products and processing, nanoingredients in food, novel foods with nanotechnology and secretive behaviour of food processing industries are the main issues in the current debate.

Stakeholder debates

There is an ongoing public and stakeholder debate on nanotechnology in agrifood, focusing on risks of engineered nanomaterials applied in food and animal feed. The interpretation of the precautionary principle¹⁶, definitions, risk assessment and labelling food products with nano ingredients are the main issues in debate. (E.g. European Parliament, BEUC, 2008¹⁷, EFSA, 2008¹⁸) According to Robinson and colleagues, this debate should be split up into more targeted debates

¹⁶ A more comprehensive overview of the different interpretations of the precautionary principle is given in Malsch & Hvidtfelt-Nielsen, "Individual and Collective Responsibility for Nanotechnology," ObservatoryNano, 2009, <http://www.observatorynano.eu/project/catalogue/4RC/>

¹⁷ <http://www.beuc.org/Content/Default.asp?PageID=2139>

¹⁸ http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1211902361968.htm

with specific publics such as consumers, industries (agriculture, food processing) etc. The organic foods industry is a particular niche market critical to nanomaterials (c.f. the ban on nanomaterials issued by the British Soil Association in 2008)¹⁹, which should be engaged in the debate. (Robinson et al, 2010)

In 2008, Friends of the Earth stirred up debate on nanotechnology in agrifood by its report “Out of the Laboratory and Onto Our Plates.” They called for a moratorium on the further commercial release of food products, food packaging, food contact materials and agrochemicals that contain manufactured nanomaterials until nano-specific safety laws are established and the public is involved in decision making. Nanomaterials must be regulated as new substances. The size based definition of nanomaterials must be extended to particles up to 300 nm. Transparency in safety assessment and product labelling is essential. Public involvement in decision making is required. Support for sustainable food and farming is needed. (Miller & Senjen, 2008)

Agricultural technologies

The European Group on Ethics in Science and Technology (EGE) formulated an ethical framework for agriculture which could be used to evaluate trends in agricultural technologies including nanotechnology. New technologies for agrifood applications should contribute to:

- Food security;
- Sustainable use of resources and fair trade at world level in agricultural products; and
- Ethically sound design of sustainable EU agricultural policies.

The challenge for the 21st century is to make the transition from industrial/production agriculture to agricultural sustainability and food security. In such a sustainable agriculture, stewardship of the land, preservation of resource base and biodiversity, health of farm workers, the value of rural communities and of the agricultural landscape, are important.

The European Charter of Human Rights (2000) is the basis for deriving ethical goals for responsible action in agriculture, based on two fundamental ethical principles:

- 1) Respect for Human Dignity²⁰: this implies the fundamental human right to food, the need to respect individual freedom, self-determination and well-being.
- 2) Justice: implying distributive justice (guaranteeing the right to food on an equitable and fair basis), social justice (protecting the most disadvantaged in society), equal opportunities (guaranteeing fair trade), and intergenerational justice (safeguarding the interests of future generations).

Other relevant principles are solidarity and the precautionary principle.

The EGE is in favour of promoting innovation in agriculture as long as the technologies contribute to the ethical goals food security, safety and sustainability, but warns that technological solutions should be complemented by other measures. The introduction of new technologies should be accompanied by impact assessment studies comparing impacts on environmental and social impacts of existing solutions with expected impacts of the new technologies. EU food safety standards should be based on scientific data only and if they differ from international standards, this must be scientifically justified. New technologies could contribute to preservation of agricultural biodiversity, soil and water protection, the development of biofuels which do not conflict with food security, and reduction of recycling of food waste, among others. Modern agricultural research should follow an integrated approach and measures should be taken to stop the brain-drain of European researchers. They recommend public participation as well as reconsideration of current trends in IPR policies for plants. (EGE, 2008)

¹⁹ See <http://www.soilassociation.org/LinkClick.aspx?fileticket=Moyw3Q7H%2Fp4%3D&tabid=303>

²⁰ See also EGE Opinion 20 on ICT implants in the human body.

In Europe, Directive 91/414/EC regulates the use of pesticides. This directive has been reviewed with the aim to decrease the number of allowed pesticides. (Robinson et al, 2010) The review has resulted in Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of the plant production products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. (OJ L309/1, 24.11.2009)

Nanoingredients in food

The Science and Technology Committee of the UK House of Lords criticised the food industry for their lack of transparency on nanotechnology in food in a report published in January 2010. Whereas the committee expected nanotechnology to bring benefits to food security and food safety, the secretiveness of the food industry about their research and products with nanoingredients was likely to raise suspicion. They urged the UK government and Research Councils to fund more research on risks of nanotechnology in food, in particular consumer exposure to nanomaterials through the gut. This research should be coordinated at an international level. The consumer should have access to balanced information on nanotechnology in food, but the committee considered a public register a better instrument to achieve this than labelling all products containing any kind of nanomaterials. (Lords, 2010)

Peter Melchett, policy director of the British Soil Association commented that “The report is good in drawing attention to the huge risks and uncertainties of nanotechnology. This is a ticking time bomb”.²¹ The consumer association “Which?” asked for clarity on what foods are using nanotechnology, focused consumer engagement on potential food developments, pre-market risk assessment and approval set out in relevant legislation for foods using nanotechnologies, mandatory labelling of materials used in the ingredients list, guidance from government, FSA and the EU to help businesses and enforcement officers understand their duties regarding nanotechnologies and food. (Which? 1 December 2009)

The UK House of Lords Science and Technology Committee appears to challenge the draft proposal for a regulation of the European Parliament and of the Council on the provision of food information to consumers which prescribes labelling food containing nanoingredients with “NANO” in the ingredients list. This proposal is tentatively scheduled for discussion in the European Parliament plenary session on 18/05/2010. (Sommer, 2009)

Novel foods

The EU Novel Foods regulation is currently being reviewed in a reading in the European Parliament. Among the proposed changes is the introduction of a category of products that consists fully or partly of engineered nanostructured materials. The European Food Safety Authority should carry out a risk assessment for the novel food and if this is accepted on the market it will be listed on the Communitarian list of Substances, published in the Official Journal of the EU. On 15 March 2010, the Council has adopted a position at first reading on novel foods, but the Commission and the rapporteur of the Parliament (29/03/2010) did not agree to part of the Council’s position. The proposed texts on engineered nanomaterials were among the contested parts. The Parliamentary committee on Environment, Public Health and Food Safety has scheduled adoption of the report in second reading on 3 May 2010, and the plenary sitting is scheduled for 5 July 2010.²² As soon as political agreement between the European Parliament and the Council has been reached, the reviewed regulation can be adopted.

²¹ <http://www.soilassociation.org/News/NewsItem/tabid/91/smId/463/ArticleID/257/reftab/92/t/Today-s-News/Default.aspx>

²² <http://www.europarl.europa.eu/oeil/file.jsp?id=5583302>

Review of relevant ethical and social science literature

A group of experts analysed the implications of lessons learned from agricultural biotechnology for nanoscience, in particular for agricultural and food applications. Nanotechnology applications in agrifood may be confronted with similar public sensitivities as those apparent in the GMO debate in Europe. Each new technology has related social, ethical, environmental, technical and economic issues. Methods for addressing these issues and standards developed for existing technologies are not necessarily suitable for the new technology. The different stakeholders discussing nanotechnology have contending perspectives on how their introduction should be governed. Nanotechnology for agrifood applications raises particular privacy issues related to RFID chips and other remotely readable tags for cattle (privacy of the owner) and food products (consumer privacy). New hazards in the form of nano(eco)toxicity may also be introduced. Nanotechnology is mostly not alive. Therefore many concerns with biohazards are not relevant to nanotechnology for agrifood applications. (David & Thompson, 2008) Related to this, Busch (2008) considered the future of nanotechnology in agriculture to be uncertain, because it is a relatively less profitable sector than other application domains, and companies and researchers are afraid of a similar public reaction as to GMO's. There is a shortage of relevant skills among researchers and adequate regulatory structures for governing the technology are lacking.

More specific, Evers et al (2008) welcomed nano-enabled diagnostics for livestock disease control, as it may contribute to more use of vaccination rather than culling infected animals to stamp out epidemics, and balance the autonomy-paternalism dilemma between farmers and authorities. They have applied biomedical ethical criteria non-maleficence, beneficence, autonomy and justice to the case.

Another relevant trend in general ethics of agrifood was highlighted by Busch (2009). In the food sector, private governance and standardisation involving direct dialogue between industry and NGO's are increasingly replacing government regulation. He examined the ethical implications from consequentialist, deontological and virtue ethics perspectives. Similarly, Thompson (2008) proposed to return to the tradition of agrarian ethics in the contemporary environmental ethics debate including pragmatism and virtue ethics. Agrarian ethics combined the influence of nature, climate and soil with social and political institutions in moral character formation.

Conclusions

Whereas according to some experts nanotechnology has the potential to contribute to food safety & security, sustainable use of resources and animal welfare, this is contested by others. Stakeholder concerns include consumer choice and transparency regarding products and processes using nanotechnology in the food sector. These issues are high on the stakeholder and political agenda in Europe. NGO's are concerned about the absence of nano-specific safety laws and the lack of public involvement in decision making. Political decision making on nanotechnology in novel foods and nano-labelling of food products is in progress in Europe, but controversies appear to remain especially related to the novel food regulation.

Ethicists and social scientists explored similarities and differences of nanotechnology and GMO's in agrifood. The different stakeholders discussing nanotechnology have contending perspectives on how their introduction should be governed. Company's fear of a potential public backlash may inhibit nanotechnology innovation in agriculture and food. The trend that government regulation is increasingly replaced by governance involving debates by stakeholders may have unforeseen societal

consequences. Nanotechnology for agrifood applications raises particular privacy issues related to RFID chips and other remotely readable tags for cattle (privacy of the owner) and food products (consumer privacy). New hazards in the form of nano(eco)toxicity may also be introduced. There is a discussion whether animal welfare would be served by modifying animal properties or incorporating sensors and devices in the animal body.

The EGE ethical framework could be used to stimulate balanced reflection on ethical issues of nanotechnology for agrifood applications. Different ethical traditions including consequentialism, deontology, virtue ethics and agrarian ethics could also be useful for this.

Animal testing

Current issues raised by technical and economic trends

On the one hand, nanotechnology is expected to contribute to alternative in vitro test methods to in vivo animal testing in biomedical research and toxicology. (e.g. Kroll et al, 2009, Bérubé, in press, Institute of Nanotechnology, 2008) On the other hand, the demand for risk assessment studies to determine toxicological risks of nanomaterials may increase the number of animal tests. (BEST, 2007, ZonMW, 2010)

Priorities in policy and stakeholder dialogue

Several key issues in the policy and stakeholder dialogue on nanotechnology were addressed in the conference on Nanotechnology and Animal Testing organised by the Institute of Nanotechnology (2008). The European Centre for the Evaluation of Alternative Methods (ECVAM) and related organisations are continuously exploring new technologies for alternative testing methods. In silico methods using computer modelling are taken into account as well as in vitro tests including those based on nanotechnology. Both in the framework of the European regulation on chemical substances REACH and in the OECD is progress in both types of methods being monitored.

Some experts emphasize that systems based thinking is important, and reductionism assuming you can use in vitro testing to predict what will happen in a living organism is flawed. Ideally, all aspects including in silico, in vitro and in vivo models should be combined in a comprehensive model. On the other hand, a systemic picture is not always needed.

Industry is already using metabolomic and genomic toxicology tests. Metabolomics is “the systematic study of the unique chemical fingerprints that specific cellular processes leave behind”. (Daviss, 2005) Genomics is the study of all the genes of a cell, or tissue. The regulatory system should reflect on the usefulness of these tests for reducing or replacing animal testing. In some cases, whole organs could be used in tests, as well as adult stem cells. So far, there is no evidence that stem cells mimic the physiological situation, but adult stem cells could give useful insight clarifying signal pathways. Human umbilical cord blood cells are also promising. The use of embryonic stem cells is controversial, but the controversy has stimulated research into less ethically problematic alternatives. Should animal testing be replaced with embryonic stem cell tests, this could imply replacing one ethical dilemma by another one.

Some experts and stakeholders agree that total replacement of animal testing by alternative methods should be the long term ambition and nothing less should be accepted. However, it requires a lot of high tech development and interdisciplinary research involving biologists as well as nanotechnologists. From an animal welfare view, total replacement should be the end goal. One argument is that animal tests are not necessarily the gold standard, as models for the human body. On the other hand, some experts don't think replacement of all animal testing is possible or even necessary, but they agree that not all currently used animal models are relevant. The focus should be on improving the relevance, by installing clinician engagement panels. The key question is to determine the appropriate level of testing. This insight on relevance should be communicated to and taken into account by technology developers making new tests, who are currently mainly working on cytotoxicity tests.

Yet others are worried that a strong focus on total replacement could take away attention from achievable short term replacement of some in vivo tests by in vitro alternatives. Also in the EU

funded Network of Excellence Nano2Life²³, in the discussion on in vitro testing, there were two schools. The pragmatists wanted to focus on demonstration and validation of existing tests for short term uptake, whereas others proposed more visionary roadmaps outlining the way forward to where we want to be in 20 years. The latter approach is considered useful for putting the technology in context. It is important to keep ethical and social aspects in mind: what and why are we testing?

There is a real chance to make substantial progress in the improvement of alternative methods. The European Commission aims to reduce animal testing in FP7 funded projects with a view to replacing it altogether (FP7 Protocol on Protection and Welfare of Animals, cited in 2nd implementation report of the European Nanoscience and Technology Action Plan)²⁴. The development of Nanotechnology based alternatives to animal testing is supported by funding projects and the discussion on adapting regulations on safety testing takes place at EU (EPAA) and OECD (WPMN) level. (EC, 2009)²⁵

Positions of animal rights organisations

A number of Animal Rights organisations have entered the debate on nanotechnology and animal testing. They tend to see both an increasing need for animal testing in Nanotoxicology and potential contributions of nanotechnology to reducing animal testing.

In the UK, the British Union for the Abolition of Vivisection BUAV²⁶ has a nuanced vision on the relationship between nanotechnology and animal testing. On the one hand, they expect that nanotechnology may provide some of the solutions to animal use in scientific research. On the other hand, this area also carries with it the risk of increased use of animals – in determining the toxicity of nanoparticles. (Taylor, 2008)

On OECD-level, the International Council on Animal Protection in OECD Programmes ICAPO²⁷ aims to promote the use of alternatives to animal testing in OECD guidelines. Their concerns include the current OECD programme on nanomaterials.

In Switzerland, the Foundation Animal Free Research²⁸ funded a literature survey on animal and non-animal experiments in nanotechnology in 2008 (Sauer, 2009). In 2009, this research is continuing by putting the results of the survey into practice, and attempting to prevent the use of animal experiments in risk assessment of nanoparticles in the EU Member States and Switzerland. (AnimalFreeResearch website, 2009)

In The Netherlands, a Societal and Scientific Trend Analysis on Animal Testing highlighted possible increasing needs for animal testing in risk assessment of nanomaterials, but also referred to promises that nanotechnology in labs on a chip could contribute to reduction or replacement of animal testing. (ZonMW, 2010) The Dutch Animal Rights organisation AVS Proefdiervrij pleads for developing applications of nanotechnology in alternative toxicity tests for animal testing²⁹. Unilever has taken the initiative Assuring Safety without Animal Testing (ASAT). Since 2005, Unilever, the Funding Council for Health Research ZonMW and the Royal Dutch Academy of Sciences KNAW have convinced the Ministry of Healthcare to invest in the ASAT initiative³⁰. This research programme worth €1.2 million has been carried out in 2008 and 2009. The ASAT Foundation, supporting the ASAT Initiative, was launched end of 2008.³¹ (Sangster, 2009)

The Dutch Animal Protection organisation (Dierenbescherming) pleads for the 3Rs (Refinement, Reduction and Replacement) of animal testing, and is concerned that the government invests

²³ <http://www.nano2life.org/content.php?id=29>

²⁴ http://ec.europa.eu/food/animal/welfare/actionplan/actionplan_en.htm

²⁵ http://ec.europa.eu/nanotechnology/policies_en.html

²⁶ www.buav.org

²⁷ <http://www.icao.org/index.html>

²⁸ <http://www.animalfree-research.org/e/home.html>

²⁹ <http://vereniging.proefdiervrij.nl/client/1/?websiteid=1&contentid=1621&pagetitle=Nanotechnologie>

³⁰ <http://www.asat-initiative.eu/>

³¹ <http://www.asat-foundation.org/>

substantially more in animal testing than in alternatives. Nanotechnology is not explicitly mentioned in their position.³²

Review of relevant ethical and social science literature

Ursula Sauer (2009) has reviewed literature based on in vivo and in vitro tests in nanotechnology. A total of 164 articles from Germany, France, the UK, Italy, the Netherlands and Switzerland published between 2004 and 2007 including animal tests were analysed. The articles covered studies in nanomedicine as well as toxicity tests for nanomaterials. Many experiments were moderately or severely distressful to the animals, but the research in which the animals were experimented upon is also expected to bring moderate to high potential benefits. The article includes also a broad range of non-animal test alternatives enabled by nanotechnology and other techniques. It appears that there are only explicit incentives for avoiding animal testing in Nanotoxicology, but not in nanomedicine. The article calls for a change of paradigm towards founding biomedical research on non-animal test results.

In another article, Sauer (2009a) examined political incentives towards replacing animal testing in nanotechnology in Europe. She found that the requirement in the Lisbon Treaty that the EU and its member states should consider animal welfare issues in new policies is partly being implemented. It is included in action plans, and funding is available mainly for non-animal Nanotoxicology test methods. It is considered insufficient to bring about a paradigm change in toxicology in biomedical research. Animal welfare issues should be addressed in ethical deliberations on nanotechnology which influence policy decisions. Public dialogue should take into account information on resulting animal testing.

Earlier, Arianna Ferrari (2008) argued that two main challenges need to be resolved before nanotechnology can make any contribution to reducing, refining or replacing animal testing. Firstly, the knowledge gained through nanotechnologies should enable overstepping the stage of animal in vivo models in life sciences. Secondly, there is a need for ethical investigation on the goals of nanotechnologies and the legitimacy of experiments for new products.

Conclusions

Several new technologies which may be used in alternative testing methods are being explored, including some based on nanotechnology. According to some, there is a real chance to make substantial progress in the improvement of alternative methods, thanks to EU and national funded projects. Animal rights organisations tend to take nuanced positions towards nanotechnology and animal testing, but plead for more incentives to avoid animal testing also in (nano) biomedical research. Some are sceptical about the chances that nanotechnology may at all contribute to reduction or replacement of animal testing.

Broader context

Of course, nanobioethics does not exist in a vacuum, but is part of a broader movement to improve ethical reflection and governance of life sciences for healthcare and food production. Several contemporary authors have made proposals for improving such governance in relation to nanotechnology. The general trends in this debate are ethical reflection and research into ethical,

³² <http://www.dierenbescherming.nl/alternatieven-dierproeven>

legal and societal aspects (ELSA) of nanotechnology by experts, and public engagement projects. The work of philosophers and social scientists can be subdivided in assessment of scenarios and visions which inspire research and development activities and policies, and speculative ethics exploring potential long term future implications. Public engagement activities include attempts at democratising science. Recent trends are to focus more on upstream and midstream engagement. Upstream engagement indicates dialogue between scientists and lay persons in more basic research phases, and midstream engagement in more applied research phases. Robert (2008a) recently published a more extensive review on nanoethics literature.

Kaiser et al (2010) opened a novel line of arguments asking how nanobiotechnologies actually are and how they should be assessed. Technology Assessment is more than ethics but nanobioethics clearly has a leading role in ELSA programs. Leach Scully and Rehmann-Sutter distinguished between different conceptual frameworks of nanobioethics and discussed them in a comparative perspective: 1) The acceptability frame, 2) the desirability frame, 3) the novel ethics frame, 4) the governance approach, and 5) the sociotechnical systems perspective. They concluded that the last and most comprehensive approach to nanobioethics (sociotechnical systems perspective) has some key advantages. It fundamentally criticises technological determinism and adopts a practical perspective on technology itself. There, the ethical questions arise in the context of a discussion about which kind of world should be constituted through technological practices. The key references for the sociotechnical systems perspective are Deborah Johnson (Johnson & Wetmore, 2008) and Arie Rip (e.g. Rip, 2008).

Seen from the perspective of comparative nanobioethics the present report is bound to the acceptability and desirability frames, with some excursions into governance and novel ethics. But the sociotechnical systems perspective is underrepresented. This however mirrors the landscape of the current publications.

Acceptability and desirability of nanobiotechnology are discussed by authors including Siep and Khushf). Siep (2008) distinguished lay ethics and professional ethics in the debate on ethics of nanobiotechnology. Not only the general public but also natural scientists lack understanding of professional ethics and therefore need to be educated in order to be able to appreciate the contributions ethics can make to the discussion on nanobiotechnology. He furthermore distinguishes long term and short term issues of nanobiotechnology and focuses on ethical issues of micro-implants. Similarly, Khushf (2007) pleaded for midterm ethical reflection on nanobiotechnology, between focusing on short-term issues and long term speculative ethics.

As an example of the novel ethics approach Swierstra & Rip (2007) analysed ethical and moral argumentation in the public debate on nanotechnology including consequentialist, deontological and virtue ethics. They saw nanoethics as a special case of ethics of New and Emerging Science and Technology (NEST-ethics) and pleaded for the competitive arena model of public debate rather than the agora model aiming for consensus on the morally “best” solutions. Their analysis included nanobioethical issues including human enhancement and nanobiomedical technologies. Dupuy (2007) recommended that nanoethics should confront the great questions of moral philosophy.

The governance approach was followed by other authors. Grunwald (2004) proposed prospective risk assessment of nanobiotechnology. Nordmann (2007) analysed conflicting claims of societal benefits of converging technologies originating from the USA and Europe and recommended that scholars in Social Studies of Science should help disentangle premature claims. Robert (2008) pleaded for a new social contract between nanoscientists and society to overcome the controversies surrounding nanosciences and nanotechnologies. Nordmann and Rip (2009) considered it important to reflect on the ethical issues of nano and other emerging technologies, but pleaded for avoiding speculative ethics disconnected from research that is currently taking place.

Retèl et al (2009) found a lack of systematic Health Technology Assessment or Constructive Technology Assessment studies on nanotechnology in oncology. Evaluation of financial and organisational aspects is the most important aspect that is missing in existing studies.

Conclusions

In this report, a technology centred approach was followed to ethical and societal aspects of nanotechnology for Health, Medicine, Biotechnology and Agrifood. This means that a particular subset of these broader debates among ethicists, philosophers and social scientists are selected and other equally valid discussions fall off the radar. The choice to focus on discussions closely related to current developments in nanotechnology for medical, biological and agrifood applications makes the findings of this report useful for reflection on choices by the scientific community and policy makers in science and technology policy dealing with nanotechnology. It is less suitable for decision making on priorities in public policies aimed at governing the society as a whole and targeting (nano)science, technology and innovation policy towards the long term sustainable and equitable development of our European and global societies. In this last chapter the work of some authors discussing such broader issues has been presented.

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Any opinions or predictions included in this report are solely the responsibility of the authors and can not be attributed in any way to the European Commission or other European institutions.

Annex 1: list of issues identified in technical and economic reports

The issues have been identified in ObservatoryNano reports on technical and economic trends in nanotechnology in November 2008, May and November 2009.

Table 4.1: Ethical and societal issues in the technical trend reports

Topic of the report	Identified issues
Agricultural production	<ul style="list-style-type: none"> - Sensor networks (for crops and livestock): potential ethical issues: privacy, dual use, balance security-freedom (not typical for agricultural applications); - Disease and pest control in crop plants: risks of residue and unintended consequences for human health and the environment, precaution; - Applying sensors and diagnostic devices for monitoring the physiological status of livestock: could reduce the need for “stamping out” infectious disease (c.f. Evers et al, 2008), potential benefit for animal welfare; - Intellectual property issues (proprietary technologies and knowledge may hinder innovation in e.g. nano-emulsion technology); - Genetic engineering of crops and livestock is controversial; - Agriculture as means to produce nanomaterials: competition with food-crops may lead to increased food prices and hunger (cf biodiesel), distributive justice; - Chances for green/sustainable production of (nano)materials offer potential benefits for society and the environment; - Enabling informed consumer choice for food with nano-ingredients (labelling, information); - Regulating nanotechnology in agrifood (e.g. EU Novel Food Regulation); - Improving shelf life of food by nano-enhanced packaging: sustainability, regulation /safety, privacy (RFID) issues.
Textiles technology and sector	<ul style="list-style-type: none"> - Chances for greening textiles production offer potential benefits for society and the environment (chemicals/materials/energy saving; reduced waste); - Potential unknown health/safety risks, need for life cycle analysis, precaution; - Antimicrobial applications: offers benefits as well as potential risks for health and the environment. Need for life cycle analysis, precaution; - Fear of side effects of nano-products (environmental / toxicity / allergy issues) to some extent for Clothing, domestic and medical uses (Cientifica, 2006), precaution; - Intellectual property issues (e.g. preference to licence, rather than implement) especially for medical and military uses (Cientifica, 2006); - Medical e-textiles: preventive healthcare applications change definitions of health, raising ethical issues of enhancement, choices in use of limited healthcare resources and privacy issues (also for sports).
Regenerative medicine	<ul style="list-style-type: none"> - Nanoscaffolds, tissue engineering, lab on a chip to experiment with stem cells / tissue engineering in vitro; - General biomedical ethics issues apply (c.f. NanoMed Roundtable); - Possibly enhancement issues?
Drug delivery	<ul style="list-style-type: none"> - Expected impact on the structure of the pharmaceutical industry sector:

	<p>Who gains, who pays (market failure);</p> <ul style="list-style-type: none"> - Patenting issues; - Risk management issues.
Diagnostics	<ul style="list-style-type: none"> - Nanobiosensors / nanowires: dual use medical / bioterrorism monitoring: Knowledge of suffering a disease in absence of an effective treatment; difficulties and confusion around interpreting a mass of data; - Theranostics: has potential, many questions remain (e.g. loss of control of the patient over own body).
Implants, surgery & coatings	<ul style="list-style-type: none"> - Biocompatible coatings / implant materials, electrodes in neuroimplants, battery / energy supply (transfer body heat to electricity), optical fibres for compatibility with external electromagnetic field (MRI etc), “smart knees” combined with artificial intelligence to prevent falling, implanted drug delivery system.
Novel bionano-structures	<ul style="list-style-type: none"> - Self-assembly; - Synthetic cells e.g. for drug discovery: elements, liposomes, polymers, nanoemulsions, novel fabrication techniques and nanomaterials to create cell like structures, synthetic membranes. C.f. discussion on ethical aspects of synthetic biology; - Nanosomes for cosmetics and therapeutics; - Molecular switches and molecular motors (basic research phase).
Cosmetics	<ul style="list-style-type: none"> - Nanoparticles as UV filters (TiO₂, ZnO, organic alternatives); - Nanotechnology for delivery - Risk debate, regulation, labelling (EU cosmetics regulation will be in place from 2012?)
Construction sector	<ul style="list-style-type: none"> - Precaution (worker safety)? - Use of raw materials / commodities markets? (Sustainability, distributive justice); - Sustainability issues, incl. energy saving, emission reduction in manufacturing building materials or in use; - Cooperation with or impact on socio-economic development of developing countries, distributive justice
Security	<ul style="list-style-type: none"> - Focus on terrorism, excluding other security issues including warfare and crime (but includes narcotics); - Dual use is acknowledged (detection of chemical agents incl. industrial toxins); - Cf HIDE project discussion of biometrics / Nanoforum report on nanosecurity – elsa issues; - Terahertz detectors lead to severe privacy and human rights issues if used to see through clothes of people; - What is the main market for security technologies (small shop-owners wanting to prevent theft?). - Personal Protective clothing / equipment for first responders (NBCR, firefighters): no ELSA issues identified (November 2009 report)
Environment – groundwater remediation	<ul style="list-style-type: none"> - Potential benefits for sustainable development; - Life cycle analysis needed to avoid unintended consequences, precaution. - Field testing of nZVI: uncertainty about risks, possible conflicts with stakeholders (Nov 2009 report)
Environment – chemical and gas sensor	<ul style="list-style-type: none"> - Privacy issues; - Other ethical or ELSA issues depend on the application.

Chemistry & materials	- Precaution , risk governance
ICT- Displays	- Ubiquitous computing issues (privacy); - Human-machine interactions; - Life cycle analysis, precaution .

No issues were identified for ICT – Power components, Energy (incl. solar cells), Automotive & Aeronautics.

Table 4.3 Nanobiomedical ethics
<ul style="list-style-type: none"> - Human machine interaction; - Enhancement; - Anthropology; - Human rights; - Health or medical ethics; - Bioethics.

Annex 2: relevant issues in policy / stakeholder debate

Topic	Organisations	weblinks
Synthetic Biology	European Group on Ethics (2009), Rathenau Instituut, ETC group, Kavli foundation, KNAW / COGEM, NL govt.	http://ec.europa.eu/european_group_ethics/index_en.htm www.rathenau.nl www.etcgroup.org
Human Enhancement / Converging Technologies / Brain Research / Ethics of ICT implants	STOA / TAB/ Rathenau Institute, EGE, World Council of Churches, ETC group, Transhumanists, EP (Ransdorf 2006) EC (Nanocode, 2008), EP ENVI (Schlyter report, 2009) DEMOS, IEET, WIRED	http://www.itas.fzk.de/eng/etag/etag.htm ; http://www.europarl.europa.eu/stoa/default_en.htm ; http://www.rathenau.nl/ http://ec.europa.eu/european_group_ethics/index_en.htm http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//NONSGML+REPORT+A6-2006-0216+0+DOC+PDF+V0//EN&language=EN http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//NONSGML+REPORT+A6-2009-0255+0+DOC+PDF+V0//EN&language=EN http://www.demos.co.uk/publications/betterhumanscollection http://ieet.org/index.php/IEET/HETHR http://www.wired.com/wired/archive/15.01/humanintro.html
Ethics of Modern Developments in Agriculture, nanofood	EGE (2008: 3 ethical principles: food security, food safety, sustainability), nanobioraise,	http://ec.europa.eu/european_group_ethics/index_en.htm www.rathenau.nl www.nanobioraise.org

	Rathenau, EC Safety for Success	
Nanomedicine	Rathenau Institute (2004) EGE (2007), COMECE (2007), TA Swiss (2003), TAB (2003) ETP Nanomedicine ELSA board, NanoMed Roundtable	www.rathenau.nl http://ec.europa.eu/european_group_ethics/index_en.htm

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