Nanoethics (2011) 5:269–283
DOI 10.1007/s11569-011-0135-x

ORIGINAL PAPER

Ethics and Nanopharmacy: Value Sensitive Design of New Drugs

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Received: 11 October 2011 / Accepted: 21 October 2011 / Published online: 9 November 2011

Abstract Although applications are being developed and have reached the market, nanopharmacy to date is generally still conceived as an emerging technology. Its concept is ill-defined. Nanopharmacy can also be construed as a converging technology, which combines features of multiple technologies, ranging from nanotechnology to medicine and ICT. It is still debated whether its features give rise to new ethical issues or that issues associated with nanopharma are merely an extension of existing issues in the underlying fields. We argue here that, regardless of the alleged newness of the ethical issues involved, developments occasioned by technological advances affect the roles played by stakeholders in the field of nanopharmacy to such an extent that this calls for a different approach to responsible innovation in this field. Specific features associated with nanopharmacy itself and features introduced to the associated converging technologies- bring about a shift in the roles of stakeholders that call for a different approach to responsibility. We suggest that Value Sensitive Design is a suitable framework to involve stakeholders in addressing moral issues responsibly at an early stage of development of new nanopharmaceuticals.

Keywords Nanopharmaceuticals · Technological risk · Converging technologies · Ethical issue · Social impact · Value sensitive design · ICT · Nanoinformatics · Personalized medicine

This article is supported by funds generated in conjunction with a Chinese Scholarship. Code: [2006]3065

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Introduction

Nanomedicine has triggered many discussions and concerns for scientists, philosophers, ethicists and policy-makers. Nanopharmacy is a branch of nanomedicine that is already making its way out of the laboratory to the market. As an instance of converging technologies, nanopharmacy gives rise to a myriad of ethical and social issues stemming from different technologies such as nanotechnology and bioelectronics and ICT in general. Besides giving rise to pressing ethical issues, nanopharmaceutical innovations also have far reaching implications for health care in general [62]. New high tech medicines will emerge that challenge the way health care currently is practised and that call for a different approach to dealing with these ethical issues. The following examples illustrate this development.

Lab-on-a-Chip

The miniaturization in health care fuelled by nanotechnology will enable development of nanochips that are able to make multiple-parameter measurements on blood-cells and human genomes [62]. These measurements can be carried out by hand-held devices called 'laboratory on a chip'. This will make it possible to assess the (future) health status of an individual very accurately. The digital information gathered can be further analyzed by database-matching programs and statistical methods for a further diagnose. The combination of nanotechnology and ICT thus facilitates a new predictive medicine offering a personalized diagnose that can be used to tailor medical treatment and health care to the needs of the individual, so-called personalized health care or medicine (Califf 2004).

Doctor in a Cell

Limits of health care practise are further pushed by another development that is already in progress, called 'Doctor in a Cell'. The vision behind this can be summarized as 'a molecular medical team that can be injected into a patient, coursing through his bloodstream and treat it' [11]. It consists of a biological computer able to process and analyze biological signals, send out a diagnosis and even treat the patient [35]. First steps already have been taken to realize this vision. Although not working on humans, researchers have created a molecular computer that is able to diagnose defects in DNA and destroy them [11].

BioSilicon

Another example illustrates that boundaries between medical products, devices and therapies are likely to become blurred is the drug delivery system BioSilicon. BioSilicon 'is a nanostructured form of elemental silicon that is engineered to create a "honeycomb" structure of pores. This structure allows silicon to biodegrade while also allowing the retention of various drugs and vaccines within the honeycomb matrix.' [13] BioSilicon thus acts both as a drug and as a medical devise. As a result nanopharmaceuticals as BioSilicon, termed 'borderline products', no longer fit the standards currently used to identify and classify medicine [13]. Consequently concerns are raised about the suitableness of existing regulatory frameworks and testing methods of nanopharmaceuticals, as well as about knowledge gaps, questions of expertise and definition issues that the blurring of boundaries will entail.

The BioSilicon example indicates that current regulation may not be up to the challenges posed by nanopharmacy. Blurring boundaries will challenge the competence of regulatory bodies in the future as nanomedicine will continue to fulfil its promises. Although legislators, especially in the EU, do anticipate future medical innovations, for the time being they regulate nanomedical products and devices under the existing regulatory structures [13]. The general stance, most notably in the US, therefore is anticipatory and not proactive. A concern is raised that this may hamper development of nanopharmaceuticals as 'appropriate and effective regulatory structures will be critical in the successful implementation of nanomedicine and the fulfilment of its promise' [13].

Willingness to see the far reaching implications of nanopharmacy as a converging technology crossing traditional boundaries between disciplines is vital to the success of nanopharmacy. This is not only true for legislators, the same holds for other stakeholders involved in health care in general such as doctors, patients and developers of nanopharmaceuticals.

As is clear from these examples, the traditional actors involved in medical practice are not able to assess and control the technological artefacts. The burden of responsibility shifts to technological specialists involved in the design and implementation [36]. In this paper we argue that Value Sensitive Design offers a methodological stance that can help to bridge the gap between responsibility and design for nanopharmaceuticals.

We start by giving a conceptual analysis of nanopharmacy building on its emerging and converging character. Next, we discuss some fundamental developments triggered by nanopharmacy and the issues that stem from those developments. Special attention is paid to the overarching issue of dealing with these issues responsibly given the revolutionizing effect of nanopharmacy on healthcare in general. The paper concludes with a discussion on how the Value Sensitive Design (VSD) methodology can be applied to address the issues responsibly.

Conception of Nanopharmacy

We first discuss the idea of nanopharmacy by drawing upon a general characterization of nanotechnology. Nanotechnology is a multidisciplinary field of research concerned with the physical and chemical properties of chemical substances and materials on the scale of nano sized particles (from 0.1 nm to 100 nm) [5, 34]. It also studies the techniques that can be used to manipulate materials utilizing these special characteristics. The essence of nanotechnology is that new products with specifically designed target functions and special characteristics can be manufactured by means of artificial manipulation on the level of atoms and molecules. It is widely accepted by now that the application of nanotechnology will change the design and manufacturing procedures for pharmaceutical products [8, 59]. What's more, it has even been argued that the novel approach it enables will revolutionize the future of medicine [7, 26].

Nanotechnology in a short period has already brought vital changes in many practical areas of health care from the 1990's up till now. For example, in the field of diagnostics nano-chips are used to develop self tests and home diagnosis for some diseases [45]. Other applications include the use of quantum dots for more sensitive detection and nano needles which allow for surgery on nanoscale structures inside living cells and tissues without causing any damage [2]. Finally speculations about future applications predict even further reaching possibilities such as the use of multifunctional nanorobots that can operate as a self-contained entity to 'diagnoze, treat, and monitor diseases […]' [8]. Although there still are many technical barriers to overcome, these futuristic applications do raise specific ethical concerns that already attract attention in current ethical discourse.

Apart from nanotechnology, nanopharmacy integrates medicine, pharmacology, biology as well as information and communication technology (ICT). Nanopharmacy therefore must be considered as an instance of a techno-scientific complex called "converging technologies" [32]. "Converging Technologies" is a label nowadays used to point at synergies between originally separate fields leading to revolutionary innovations and thereby new impacts. Besides ethical issues associated with the individual technologies, the merger of disciplines in a converging technology issues arise that transcend particular local discourses [32, 47]. In the discussion of issues and developments below, issues stemming from individual technologies as well as the converging technology are implicated.

Although some nanopharmaceuticals have reached the market, these are still early and basic examples of applications. More revolutionary applications still lay ahead of us [26]. In this stadium it is still uncertain which of the applications and associated issues will materialize. Also the issues and applications discussed in this paper are often based on projections. We nevertheless think it is worthwhile to discuss them. Even if these specific applications and issues will never appear, they are likely to provide insights that do apply to developments that will be realized in practice [27]. Moreover, the suggested methodology for dealing with these issues is not bound by specific applications or issues, but provides a general approach to deal with human values in innovative design processes.

Like nanotechnology in general [5], at present, nanopharmacy lacks a clear, broadly accepted definition. Analogous to the definition of "nano-medicine", "nano-pharmacy" may be defined as "the uses for nanotechnology in pharmacy". Although this definition looks overly simplistic, it is all that is needed at this stage of the investigation. A too strict definition might limit the scope of (ethical) investigation to exclude important issues.

Although the fields to a large extend overlap, are sometimes used interchangeably, and are often discussed next to each other—see also our discussion below- nanopharmacy can be distinguished from nanomedicine. This can be made clear by looking at the relation between medicine and pharmacy in general. Medicines must be understood as 'therapeutics, administered to patients by clinicians', while pharmacy involves the manufacturing and researching of medicine predominantly by pharmaceutical companies [14]. This means for instance that also the translation of research into marketable medicine is a key consideration of nanopharmacy.

We think we can usefully distinguish between four perspectives to further refine our definition of nanopharmacy:

1. The materials used in nanopharmacy share specific properties that set them apart from other technologies [32], the most common property being its

nanoscale size. Apart from size, the chemical and physical properties, surface charge and shape are typically associated with nanopharmacy [5].
2. On a process level certain functions are attributed to nanopharmacy that have enormous potential in addressing the failures of traditional drugs [6]. Typically nanoparticles are mentioned as agents for (targeted) drug delivery, quantitative drugs release, imaging and diagnosis.
3. Nanopharmacy includes all the practical fields linking to nanopharmaceutical research and development (R&D), nanopharmaceuticals manufacturing, nanopharmaceuticals application and nanopharmaceuticals management.
4. Nanopharmacy is an instance of converging technologies, integrating disciplines including emerging technological fields such as nanotechnology, biotechnology and informatics.

Main Developments and Issues of Nanopharmacy

Nanopharmacy includes the research and development concerning nanopharmaceuticals, the manufacturing of nanopharmaceuticals, the application of nanopharmaceuticals as well as the management of nanopharmaceuticals. Using this broad view allows us to analyze the potential impact of nanopharmacy on health care system from the different perspectives.

In this section we discuss how technological advances in nanopharmacy as a converging technology fuel changes in the medical practice at large. By outlining these developments and the ethical and social issues implicated by these developments, we discuss how actors involved in nanopharmacy and medical practice are affected.

First the implications of nanotechnology on health practice as such are discussed together with its ethical implications, seconds social implications of nanopharmacy are discussed and finally, the implications that can be attributed more specifically to ICT as an enabler for nanopharmacy are analyzed.

Nano and Medicine

As its main constitutive technology, that sets it apart from pharmacy in general, issues associated with nanotechnology are applicable to nanopharmacy as well. Nanotechnology can be described as "[t]he design, characterization, production, and application of structures, devices, and systems by controlled manipulation of size and shape at the nanometer scale (atomic, molecular, and macromolecular scale) that produces structures, devices, and systems with at least one novel/superior characteristic or property" [6]. Working at nanoscale, ordinary materials can exhibit extraordinary properties that give rise to specific risk to cause harm [34]. Although the newness of nano-ethical issues is debated, scholars agree on a wide range of issues associated to nano [3, 9, 27, 49, 58]. Below, some of the more pressing developments and issues with respect to healthcare are described.

Revolutionizing Healthcare

Nanotechnology holds a lot of promises to medicine, although most are yet to be fulfilled. That being said, there already are many applications on the market showing us a glimpse of what lies ahead (see section Conception of Nanopharmacy). Nanomedicine is often portrayed as the future of medicine with the potential to radically change the way is practiced today [7, 8]. Improvement in the way medicine is delivered into the body, more accurate and faster diagnose and treatment of illnesses or often mentioned [8, 59]. Nanopharmaceuticals allegedly have enormous potential in addressing the failures of traditional drugs such as lack of target specificity and poor water solubility [6]. The effectiveness of drugs will increase by the ability to avoid collateral effects, for instance in chemotherapy, and use lower dosages [48]. Furthermore, nanomedicine will enable monitoring progress of medication on a person real time allowing doctors to check effectiveness of a treatment immediately [48]. Besides improving existing treatment options also new ones are created. For example, nano-particles able to pass the blood–brain barrier, a membrane which traditional drugs cannot pass, opens up 'new possibilities for treatment of psychiatric disorders, brain injuries, or even the administration of neural anesthetic' [2].

It is argued that all these and other changes will amount to 'a radical change in the basic infrastructure of the health care system, including the health care workforce' [8]. Ultimately this change can be classified as a 'shift from the hospital to the laboratory' [8]

thus fundamentally altering the health care system in a broader perspective.

Safety & Human Health Risks

One of the most significant risks associated with nanotechnology is the toxicity of nano-particles [8]. Although humans already are exposed by natural nanoparticules such as viruses and by products of combustion, the impact of manufactured nanomaterials may pose a health hazard. Reactivity of nanoparticles is depending on its size, surface to mass ratio, and bioreactivity [8]. Increased toxicity is indicated with carbon nanotubes and the application of certain metals as nanomaterial [7]. Even when substances are used that in normal conditions are not be toxic, on a nano-level alteration of its properties can imply that they become toxic. What's more, disintegration of nano-particles into smaller toxic particles may only take place after they have entered the human body [26]. So long term effects of particles may differ from those on short term. Although actual effects of nanotechnology on humans in most cases are still uncertain, it is generally accepted that use nano particles may cause health problems [2].

In relation to the use of nanomaterials for medical purposes, many concerns have been raised about conceivable toxicity of nanomedicine [2]. For instance, during treatments nanoparticles can unintentionally cause damage to healthy tissue [44]. Other concerns raised are the penetration of highly charged nanoparticles of the skin potentially damaging it and the possibility that nanoshells used to deliver drugs will accumulate in the body and cause damage [5].

Overall it is concluded that research should be done to provide more insight into the effects of nanoparticles on humans [5]. Only then a responsible trade off can be made between the health risks of applying nanomedicine and its benefits to patients as is the best practice with conventional medicine [26].

Risks Related to Diagnoses

The increase in diagnostic abilities provided by nanotechnology can cause psychosocial harms such an increased anxiety and fear about illnesses [26]. The ability to detect a single cancerous cell, for instance, 'could have profound effects upon how individuals think about the status of their health and bodies' [5]. Increased diagnostic abilities cause a heightened awareness of one's health status which could increase fear and anxiety about illness.

Besides more accurate diagnostics, nanotechnology also enables faster diagnoses and treatment. A concern has been raised that this might lead to an increase of the possibility of misdiagnoses and inappropriate treatments [26].

Finally the ability for self diagnoses that is associated with nanomedicine might result in avoidance of doctors due 'to the fear and high costs of medical assistance and treatment [26]. Although it is argued that nanomedicine will be expensive due to high development costs involved [8, 59], it is not unlikely that, parallel to other high tech products such as laptops, that once they are mass-produced the price will drop considerably. In fact, pharmaceutical companies already mention cost reduction on the long run as one of their main arguments to invest in nanotechnology [8, 19].

Re-conceptualization Issues

The introduction of nanomedicine pushes the boundaries of many of the key concepts associated with healthcare.

First, the concern is raised that as boundaries between nanotechnology, ICT, biotechnology and cognitive sciences disappear our concept of what it means to be human will change radically [16, 53]. The introduction of nano-chip implants, for instance, may enable unprecedented interactions between man and machine on a nanolevel thereby introducing a kind of hybrid humans [26]. These developments affect our view on what it means to be human [5], our human identity, and raises questions about the preservation of human dignity [26, 48].

Second, this will also entail questions on how human disease should be defined and how treatment of a disease is to be approached [5]. New diagnostic possibilities offered by nanotechnology increase our understanding of an illness and thereby raise the question of what a disease actually implies [26]. Better diagnostics also means we need to reassess the distinction between what it means to be healthy and to be ill [5]. Third, drawing a clear cut boundary between improving human capabilities and preserving existing ones may increasingly become blurred [8]. This will raise the ethical concerns about what it

means to be enhanced, whether the concept 'normality' gets a new meaning, whether society can require certain persons to be enhanced, e.g. soldiers, or surgeons, and whether focussing attention and funds on enhancement will leave certain diseases and diseased persons untreated [47]. This has drastic consequences for the conceptualization of pharmaceuticals, drugs and medicine since they are typically construed in relation to alleviating and curing disease and restoring the organism to its proper and normal function. This may change as a result of enhancing designer nano-medicine.

It is implicated that these conceptual developments will 'have a significant impact on health care professionals and patients.' [5] Not only their understanding of what concepts such as health and illness alters, also their expectations of what to expect from healthcare and their role in receiving and giving medical care may shift considerably.

Informed Consent

Regarding special characteristics of the risks for nanopharmaceuticals, another related problem must be considered, namely informed consent. Although often brought up in relation to the clinical trials of nanopharmaceuticals [48] it could also be framed as a general concern to applying of nanomaterials for medical purposes in general [9]. The notion 'informed' encompasses disclosure and comprehension of the technology being used, including any known risks and benefits [30]. 'Consent' includes voluntariness, competence and agreement of the person affected [50]. This implies that affected persons voluntarily agree to subject themselves to the technology [30]. In the light of the considerations discussed above, informed consent is problematic. As long as nanopharmaceuticals are associated with risks, but also with significant uncertainty and ignorance ("unknown unknowns"), it may prove an impossible task to inform affected persons adequately.

Harms to the Environment

The potential impact of nanoparticles on the environment has aroused concerns. For instance, quantum dots, and colloids delivering drugs may constitute non-biodegradable pollutants. They could provide an avenue for rapid and long-range transport of waste in underground water [4]. Another concern raised is that the production of nanopharmaceuticals will affect the environment in which they are manufactured causing harm to workers involved in different stages of the production process [45].

Disposal of nanopharmaceuticals may also be problematic. Even when initially harmless particles enter the environment a risk occurs. This is because after a while their chemical bond can be broke off and radicals can be recombined so that new materials are generated. Indeed, the practitioners do not know whether or not the new materials thus generated are toxic [31]. What's more the wastes for nanopharmaceuticals can be trans-located and impact other plants and animals via the food chain. For instance, iron nanoparticles can transform within ground water over a distance of 20 m and remain reactive for 4–8 weeks [18]. It is expected that current and future dissemination of nanoparticles will make unintentional exposure to them unavoidable [32].

Nanopharmacy and Society

Besides issues that affect individuals or groups of individuals, nanopharmcacy has also wider social impacts. Special institutional reform accommodating the problems discussed above needs to be realized. Plants and R&D facilities need to be designed in order to adequately deal with security and dual use issues (see [39]). Public discussions and awareness campaigns need to be started, and legislation needs to be prepared.

Push by Market and Government

An important driver behind the amount of attention and investment nanotechnology currently receives, not the least in the field of medicine is the business opportunity it is seen to offer by both private and public organizations. The pharmaceutical industry views nanotechnology as a means to 'develop methods that simplify, speed up, and reduce the costs of drug development and testing, as well as increasing drug safety and efficacy' [8]. Of significance to the public is not only the promise it hold to create jobs and prosperity, but also to make medicine more effective and widely available, thereby boosting economy and national health and life expectancy [15]. Beyond mere therapeutic applications, nanomedicine will enable forms of human enhancement that expand human cognitive and physical capabilities thereby

potentially enriching human life and wellbeing [34]. These positive prospects of nanomedicine can be traced back in investments in R&D by both public and private organizations. In the US hundreds of millions of public money is invested by the National Nanotechnology Initiative (NNI) [8], as does its European counterpart the EU Nano, Materials and Production (NMP)-program that invests hundreds of millions Euros in nano related research [25]. In the private sector it has been reported that venture capitalists and corporations are spending several billion US dollars on nanotechnology R&D globally [5]. These numbers further underline the urgency that is felt to develop and market nanopharmaceutical applications.

Social Fairness and Justice

From a cost-benefit perspective, research and development (R&D) concerning nanopharmaceuticals has a long-term cycle and consequently involves a high investment risk [61]. Acceptance of new drug formulations for instance is expensive and slow, taking up to 15 years to obtain accreditation of new drug formulas with no guarantee of success [4]. These facts indicate that nanopharmaceuticals will be relatively expensive at last in the short term. The costs may therefore increase the divide between rich and poor within and across countries [8] and contribute to unequal access to health care.

Public Backlash

The novel effectiveness of nanopharmaceuticals makes the public highly aware of the risks of nanopharmacy. In some case, uses of nanotechnology may be promoted so extensively that it becomes a hype detached from reality [5], which may occur for instance if pharmaceutical companies conceal side-effects and risks of nanodrugs in order to increase their economic benefits. A lack of understanding of the nature and impact of nanopharmaceuticals and lower level of public awareness of nanotechnology leads to irrational choices of patients and consumers. A concern is that a hype will conceal ethical and social implications of nanotechnology. Hyping nanotechnology has also the risk of backfiring. A great challenge facing Nanopharmacy then is avoiding a backlash from the public akin to that seen with genetically-modified food in Europe [40] that can slow or even halt the progress of research and development [46]. In a similar vein, a possible withdrawal of investors and market support due to a negative public opinion on nanopharmaceuticals also may hamper progress [8].

Technological Fix

The current optimism towards the possibilities of nanotechnology in general and nanomedicine in particular entails a belief that it can "fix" anything [8]. Emphasis on human ingenuity and the ability to control nature not only seem overly optimistic, but may also lead to irresponsible behaviour. The stronger the belief that nanomedicine is able to fix you, 'the less incentive there is to engage in responsible health practices, such as a healthy diet, exercise, and routine primary and preventive care.' [8]

Nontranslatability and Time to Market

Nontranslatability of researcher's ideas to large-scale manufacturing is a major issue in nanopharmacy [14]. If ideas cannot be produced at large scale, investments in R&D cannot be recovered. Requirements of translatability include repeatability of a design, stability and consistency of a new drug. These requirements set limits to which researched medicines can be actually produced and marketed at large scale. Apart from practical translatability a drug can be prevented from entering the market due to a lack of reimbursement [14]. When price per therapeutic dose or treatment become too high, cost becomes an issue. In those cases it is not worthwhile for pharmaceutical companies to invest in new drugs.

A further consideration in this respect is the time to market of a nanopharmaceutical. Even when an idea is translatable, the time to market of a new drug may be too lengthy. Manufacturers who enter the market first or second are likely to be reimbursed for their investments, and will likely have a substantial market share [14]. Those who enter the market later must have an extra edge over their competitors, for instance less side effects or better therapeutic outcome [14].

Changing Regulation

Regulations for the approval of a drug are constantly changing [14]. Pharmaceutical companies therefore run the risk of developing a drug that does not comply

with legal requirements although in an earlier stage of R&D the drug was compliant. Uncertainty about regulation is partially caused by a lack of knowledge of nanomaterials. Companies run a great risk when drugs are developed whose impacts on humans and environment are hard to quantify. On the other hand, in some cases regulators may be more flexible 'if there is a prospect of a significant improvement in the prognoses of a serious disease' [14]. Considering the huge investments needed to develop and market a new drug, uncertainty about future regulation entails a huge risk to pharmaceutical companies.

Nontranslatability and other commercial considerations indicate that societal or patient's value and commercial feasibility success sometimes can be at odds. Pharmaceutical companies have to evaluate at each stage starting at the research stage of a nanopharmaceutical whether continuation is commercially feasible. Outlook on reimbursement therefore should be at the heart of any evaluation of nanopharmaceuticals.

Nano, Medicine and ICT: Developments & Issues

As informatization and miniaturization go hand in hand, the relationship between nanotechnology and ICT must be seen as twofold [53]. On the one hand nanotechnology is a crucial enabler to the development of computers on a nano scale that will be much more powerful than any computer we have at this point in time [61]. On the other hand are the possibilities of nanotechnological applications such as in nanopharmacy greatly enhanced by the possibilities offered by computers [1]. Computational techniques can be used as intrinsic part of a nanopharmaceutical or as an external counterpart used to analyse and process data gathered by the nanopharmaceutical. Nanoinformatics, which operates at the intersection between informatics, nanotechnology and medicine, refers to 'the use of informatics techniques for analyzing and processing information about the structure and physico-chemical characteristics of nanoparticles, their interactions with their biological environments, and their applications'[1]. One of the goals of nanoinformatics is to structure information in nanomedicine to make it more widely available. One way to realize this, for example, is by integrating data from nanomedical-sources in Electronic Health Records (EHR) [1]. Another is to apply knowledge extraction techniques such as data mining and text mining on the data collected. It is anticipated that in the (near) future ICT techniques such as data mining and combining data from different sources will become part of nanopharmaceutical services offered to medical professionals but also (directly) to patients or customers [1]. Finally the integration of nanopharmacy with grid and cloud computing is an important development as it introduces new ethical issues that are related to the use of grids and clouds, and also exacerbates issues already associated with nanomedicine [1].

Personalized Medicine

One of the most striking developments in this respect is the contribution of ICT enabled nanotechnology to personalized medicine [1]. It is anticipated that in the next 10 to 15 years the diagnostic and therapeutic advancements made possible by nanomaterials will enable custom treatments to specific individual needs [7]. A fundamental shift in the model of medicine will take place. Instead of reactive model of medicine geared towards diagnosing and treating acute diseases once they develop, increasingly a proactive model of medicine will become dominant that anticipates illnesses by deploying predictive and preventive measures [8]. For example, it is suggested that nanomedicine will make it possible to create a regenerative medicine that can repair human tissues to treat diseases and injuries [44].

Currently personalized medicine still is in its early stages of development and not well defined yet. Also, it is unclear how much investment is needed and what the costs of actual implementation will be [8]. Despite uncertainty surrounding it, technology advances and economical prospects indicate that personalized medicine in one form or the other will be realized some day. What is clear though is that developments such as personalized medicine have a profound potential to reshape healthcare as we know it today.

Pharmacogenetics: Patient and Disease Stratification[1]

An important enabler and forerunner of truly personalized medicine is pharmacogenetics. Potential possibilities

[1] We thank an anonymous reviewer of the journal for the valuable suggestion to draw a comparison of nanopharmacy with pharmacogenetics.

and risks associated with pharmacogenetics therefore carry over to personalized medicine and nanopharmacy. Pharmacogenetics enables the replacement of general applicable medicine by medication tailored to the specific genetic traits of a patient [24]. Possible improvements that this technology entails include increasing medical effectiveness, decreasing adverse drug reactions and lowering health costs [43]. Pharmacogenetics may also affect the value of justice in two ways [52]. On the one hand it facilitates the identification and use of difference between individuals and leads to more justice as it enables a way to overcome moral differences amongst patients and thereby offering them the same care. Especially variations in safety and efficacy of medications vary between individuals. Connecting genotype to such variations make it possible to make a trade-off between these two values per genotype instead of an entire population. On the other hand pharmacogenetics may lead to injustice in two following ways: 'through the inappropriate use of the differences identified by pharmacogenetics or, through the inappropriate failure to use such differences'[52]. Stratification of patients for instance may exclude certain small genetic subgroups -so called 'orphans'- from getting proper therapy as their group is too small for commercial exploitation [24].

Furthermore, pharmacogenetics may only be accessible for the rich thus excluding the poor. For one, only health care systems 'with significant resources and good infrastructure will be able to use the technology'[24]. Because pharmacogenetics may produce significantly better results than the traditional drugs that are accessible to (some of) the poor, inequality in healthcare does entail inequality more broadly as well [24]. Besides the benefits, the risks created by pharmacogenetics may be unequally distributed between genetic sub-groups as well [52]. As drugs are developed and tested specifically for a certain genetic sub-group, other groups excluded from trials run a risk for instance 'in the event of inadvertent or inappropriate off-label prescribing'[52]. Lastly, genetic stratification may lead to discrimination and stigmatization of certain groups that share specific traits such as a poor response to certain medications [52].

Costs of Healthcare

Depending on its innovativeness, generally costs of introducing a new pharmaceutical product will be several hundred million US dollars [5]. Although prices paid by consumers or patients over time will steadily drop, initially nanopharmaceuticals will be costly since companies have to recover substantial investments [8]. Personalized medicine for example may prove to be a financial burden as it stimulates the use of costly preventive approaches [1]. On the positive, it is also claimed that nanotechnology will make certain processes faster and cheaper [8]. Also use of information technology may help in planning and allocating resources more efficiently, for instance by identifying patients that will benefit from a specific nanomedicine, so they can be targeted more cost effectively [1]. Moreover, it is also argued that nanomedicine on the longer run will reduce societal and economic costs associated with healthcare and improve clinical outcomes for the patient at the same time [5]. Like with other mass produced high tech products, scaling up the production of nanopharmaceuticals will lower the prices rapidly.

Changing Roles in Medicine

Nanotechnology in general is attributed disruptive qualities. Other products and processes are put under pressure to realign themselves around it [8]. Consequently it potentially transforms such things as social relations, labour, economies and institutions [8]. This also holds for nanomedicine. It is argued that it will revolutionize the healthcare system and the practice of medicine in an unprecedented way [26], dwarfing 'all other trends in the history of medical technology' [38].

One trend is the change in the roles of individuals in the health care system. Technology will empower patients and increase control over their life [1]. Personalized medicine for instance enables patients to diagnose and treat themselves without consulting medical practitioners. An anticipated effect is that people will become and should become to a greater extent responsible for their decision making (Califf 2004). Based on the detailed information offered by medical devices about their health status they should be able to make rational choices concerning their healthcare. This raises the question whether more autonomy leads to better healthcare: i.e. will a patient be able to make good decisions. The fact that a body and its disease are not a singular matter makes diagnosing and treatment a complex and messy thing,

that is not easily caught in generalized principles [41]. What's more, even if technology enables us to do so, this doesn't mean that patients will. Mol argues that while autonomy is an important moral value, it is no goal in itself. Good care may involve restricting patient's autonomy in favour of trained professionals such as doctors [42]. Furthermore, what amount to good care or the better treatment is not always straightforward. Treatment of diabetes patients for instance may involve a trade-off between a longer life, or a life lived more intensely [42]. It may prove to be a daunting task for a patient, or even a doctor, to interpret the information offered by nanopharmaceutical devises and apply them to their specific case while taking health, moral and social implications into consideration.

An increase in the contribution of technology in healthcare processes is likely to be accompanied by a decrease in the influence of medical specialists. As systems become more complex, it is harder for an individual specialist to combine the competences needed especially specific technological expertise [32]. In a converging field such as nanomedicine that covers a range of specialized technologies, this will be even more so, especially for traditional medical professionals that lack any training in these disciples. What's more, personalized medicine adds to the autonomy of patients at the expense of medical professional's influence [48]. The influence of doctors on patients is further diminished by reduction of personal interaction cause by technology [48]. In all, the role of medical professionals may alter considerably due to introduction of advanced nanopharmaceutical products. Also, increasing importance of ICT and nanoinformatics in medical practise will entail a more substantial role for computer scientists not just in research and development of new nanomedicine, but in (supporting) implementation as well, for instance in knowledge management or actual lab work [1].

Data Overflow

Fuelled by the success of the internet, an enormous amount of (bio) medical information has become available for practitioners, researchers, patients and the public in general [1]. The enhanced diagnostic capabilities of nanopharmaceuticals promise to push these boundaries even further by enabling more accurate and detailed monitoring. The concern is raised that this explosion of the amount of medical data may 'eventually overwhelm the ability of health information systems to evaluate it—making effective treatment impossible' [5]. As the amount of data generated may prove to be too vast for individuals to reach a timely diagnose or diagnose at all as it becomes harder to separate relevant data from the irrelevant, support by ICT, such as data mining tools, will become vital. Again, this development indicates an increase in dependency of medical practitioners on technology. Below we will argue that this dependency entails a shift of control and responsibility from traditional medical professionals and patients to computer scientists and other technical experts.

Privacy

The diagnostic and surveillance [56] possibilities of nanotechnology combined with ICTs raise concerns about privacy. For instance, monitoring by a implanted nanochip brings up the question of who has access to the data collected and for what purposes this data is been used [26, 37]. The usage of biometrics and ICT implants "anytime and anywhere inherits that too many people, state authorities, or even companies will know too much about us. There will be too many opportunities to use personal related information against us" [60]. For instance, interception of sensitive data by health insurance companies or employers could affect 'insurance coverage, employment, or other social conditions where privacy and confidentiality of patients is paramount' [1]. In general privacy is the number one ethical concern in ICT enabled contexts [29]. When medical data is involved this issue becomes even more pressing as people are especially sensitive about their medical data. The combination of nanopharmaceutical applications and grid or cloud computing, both suspect to give rise to privacy concerns, therefore needs extra careful evaluation with respect to privacy issues.

Other Concerns

Besides privacy concerns, the close collaboration between nanotechnology and other ICTs will introduce or exacerbate a myriad of ethical issues that are associated to ICT in general. The value of autonomy will be at stake as control over medical data shift from local records to the cloud. This development will also

raise questions about security of data and trust in service providers who handle the data [54]. Another issue is related to Intellectual Property (IP), namely who will own the medical data? [33]. The convergence of medical practice with nanotechnology and ICTs like cloud computing, AI and robotics thus intensifies the need to address these ICT related issues as the fields become more intertwined.

Shift of Responsibility to Address Issues

Being at the intersection of disciplines, nanopharmacy inherits ethical concerns that its underlying enabling technologies entail. Convergence exacerbates existing problems and in some cases introduces new ones. As technology moves forward, and millions of dollars are invested and expectations rise, issues will have to be addressed and resolved. At the same time, developments in nanopharmacy radically change the health care system to such an extent that addressing these issues becomes problematic. Personalized medicine, for instance, enhances the autonomy of the patient and user by giving them more control, but at the same time shifts responsibility and liability to the service providers and product developers because medical professionals slowly move out of the picture. What's more, convergence of high tech disciplines makes it increasingly difficult for specialists in one field to assess the work of others also involved in the process. In all, medical professionals but also patients will be less able to assess the workings and output of nanopharmaceuticals and must rely on its workings as they are designed into them. The developments outlined indicate a shift towards the designer or engineer as a responsible agent in the healthcare at the expense of traditional medical practitioner, calls for a new reveille: a design turn in ethics [55].

Instead of conducting an ethical analysis and evaluation after a drug has been designed or taken in production, it should be incorporated into the design phase of a new drug. In this way designers and producers of nanopharmaceuticals can take their responsibility to address ethical issues implicated. This will also lower the risks of investment as possible hiccups in the introduction of a new drug due to moral concerns are addressed beforehand.

Design Turn in Ethics: Designer Nanodrugs

So far we have been analysing nanopharmacy with respect to main developments and issues that are implicated in these developments. We showed that multiple ethical and social issues arise that need attention. Also it became clear that the traditional way of addressing these issues is becoming problematic as the roles and stakes change due to the developments instigated by technological advances. In this section we suggest a methodology that does justice to this shift of responsibility in addressing ethical issues to an earlier stage in the life cycle of nanopharmaceutical, namely Value Sensitive Design (VSD). Although it originates from the field of Human Computer Interaction (HCI) over the years VSD has spread to other a range of other fields, often specialized branches of ICT such as Affective Computing [51] and Augmented Reality [22]. It supports hands-on development of high tech products while taking social and ethical issues into account. This methodology therefore is particularly fit to support design processes that couple dynamic and rapid development to uncertainty and urgent ethical concerns as the field of nanopharmacy does.

VSD starts from the premise that technology applications are non-neutral or value laden in the sense that they have a political or morally relevant impact on individuals and society [57]. Acting in accordance with moral values such as freedom, equality, trust, autonomy or privacy justice is facilitated or constrained by technology [21]. Where other design frameworks focus on functional requirements such as usability, efficiency or speed, VSD primarily and specifically focuses on values and requirements of moral import. More specifically it aims at reconciling different and opposing values in engineering design or innovations [57]. Typically ethical and social issues associated with a technology application are related to certain social or moral values that the technology embodies. By analysing the value and operationalize it into the design, ethical issues can be addressed in the design phase.

VSD does not aspire to offer a full-fledged design methodology. Rather it must be viewed as a tool that augments design processes that already exist [12]. Because VSD follows a pattern that is generally used by often used engineering approaches, it can be easily incorporated into already established design processes

[12]. Integration of VSD in design practice in Nanopharmacy would therefore require a thorough understanding of methodologies used for nanopharmaceutical design. By evaluating specific traits and needs of current design practice, typical stages of VSD such as conceptual and empirical investigations can be applied to meet those requirements. Conceptual investigation would typically involve researching values associated with ethical issues discerned.

A natural starting point would be the four well-established ethical principles of healthcare: autonomy, beneficence, non-malfeasance and justice [1]. These values indicate both positive value contribution that drugs can deliver to patients, as well as many concerns outlined in section Main Developments and Issues of Nanopharmacy for instance about safety, health risks, environmental issues and a variety of social issues.

An example in nanopharmacy which forms a clear exemplification of the design for values perspective is development of a nanoparticle cancer therapeutic. Throughout this process tradeoffs must be made between safety and efficacy. Safety would entail not causing harm, not leaving residues or not causing detectable biological changes in the patient at any level [14]. Efficacy indicates to what extent the drug succeeds in eliminating cancer cells. One of the parameters affecting efficacy is the amount of toxicity of the particle as the toxic nanomaterial is needed to kill cancer cells [20]. This depends on the choice of drug and the therapeutic dose used. On the other hand toxicity also is potentially harmful to a patient's healthy tissue as well as to the environment when released from the patient's body. In balancing the implicated values in these tradeoffs, moral justification of valuations is required. The VSD offers methods to conceptualize and operationalize the values implicated by consulting ethical literature, engaging stakeholders and assessing technological possibilities.

As ICT is a major enabler of the new nanopharmaceutical drugs also values implicated by ICT need to be considered. Foremost privacy and data security issues should be addressed as the nanopharmaceutical is likely to produce personal medical data that needs to be analysed and interpreted by software probably on a different location than the patient. This may also involve storing data in a grid or in the cloud as complex data mining techniques or large scale data comparing is required. Using ICT thus on the one hand contributes to the human value of beneficence but on the other hand may also have a diminishing effect on the autonomy or privacy of a patient. Actual investigation would require drawing on available relevant ethical analyses. Literature by multiple authors [12, 23] offers good examples on how to commence such investigations.

VSD can also assist researchers and developers in a pragmatic way to comply with the code of conduct for responsible research in Nano science and nanotechnology adopted and proposed to the Member States of the EU by the European Commission in 2008 [17]. Amongst other principles it calls for inclusiveness and openness to all stakeholders, for accountability of researchers and researchers organisations and 'for social, environmental, and human health impacts that their Nano science and nanotechnology research may impose on present and future generations.'[32] Stakeholder involvement is a key feature of VSD. In the conceptual investigations stage for example it is considered how the technology could both socially benefit and negatively impact stakeholders. Both direct and indirect stakeholders should be considered by the designers. Stakeholders who interact directly with a technology are defined direct stakeholders, while those who are peripherally connected to the technology are indirect stakeholders [12]. In case of nanopharmacy patients receiving the medicine and medical professionals involved would be the direct stakeholders while bystanders, the public in general, pharmaceutical companies and companies providing additional services such as cloud providers would count as indirect stakeholders. By connecting the values discerned to specific stakeholders a more specific picture is painted of the impact of the nanopharmaceutical. In this evaluation also economical cost and benefits as well as and social costs and benefits such as public health costs can be taken into account.

By aligning current testing practice with empirical research methods proposed by VSD existing trajectories of testing nanopharmaceutical can be improved. Testing a pharmaceutical is bound by strict legal standards such as the regulatory framework by the Federal Drugs Agency (FDA) in the US [6]. Concerns have been raised about gaps that exist in what currently is legally required in medical testing [28]. Integrating VSD in testing practise could contribute to covering these gaps. Nanopharmacy as a converging

technology may entail new issues or at least existing issues and implicated values need to be reassessed as technological advancements and convergence exacerbate current issues [5, 16, 32]. Integrating testing practises could lead to a broader and more thorough testing of nanopharmaceuticals. For one, values implicated by nanopharmacy as a converging technology thus including values stemming from enabling technologies would be evaluated. Secondly, more justice would be done to the specific characteristics of nanotechnology itself, for instance by introducing post-marketing surveillance (Phase IV) studies [26].

Actual implementation of VSD requires detailed insights and information of nanopharmacy and medical practice in general. This means researchers and other specialists in the field of nanopharmacy need to be involved in the process of refining VSD to specific requirements at hand, integrating it in existing methodologies and finally actually implementing VSD. The theoretical groundwork and practical experiences on VSD that have been build up over the last decade provide a rich source to draw upon in further exploration of a value sensitive approach in nanopharmaceutical design.

Conclusions

The introduction of nanopharmaceuticals poses new challenges for the medical health system. Technological innovations fuelled by nanotechnology not only give rise to many pressing ethical and social issues, they also affect the way issues can be addressed. In this paper we explored how Value Sensitive Design offers a way to bridge the gap between ethics and design needed to address ethical issues before nanopharmaceuticals reach the market.

Using a broad conception of nanopharmacy, i.e. as 'the uses of nanotechnology in pharmacy', allows us to assess the impact of nanopharmacy on health care in general, and prevents ethical issues from being excluded from the analysis. By framing nanopharmacy as an emerging technology and an instance of converging technologies the inherent uncertainty and complexity of nanopharmacy is taken as a starting point of further investigation. Nanotechnology and ICT as enabling technologies of nanopharmacy introduce ethical and social issues such as health and safety risks, environmental risks, conceptual concerns and possible infringement of privacy and autonomy. Furthermore, convergence of these and other technologies in nanopharmacy is likely to exacerbate these issues and bring new issues to the table. Besides these concerns, ICT and nanotechnology also instigate developments that fundamentally change how healthcare is practised today. The rise of personalized medicine and the further enmeshing of pharmacy with emerging ICTs such as grid and cloud computing affect the roles of both patients and medical professionals such that it becomes more difficult for them to deal with ethical issues in medical practise responsibly. Technology makes pharmaceutical more specialized and complex and therefore less assessable and controllable by non experts. Next, innovations fuelled by nanotechnology such as personalized medicine, decrease the interaction between patient and medical professional, shifting responsibility of medical practise to producer or developer of nanopharmaceuticals. These developments in combination with challenges posed by social and ethical issues call for an approach that supports dealing with these issues during the design of nanopharmaceuticals so before they reach the market or used in medical practise.

The Value Sensitive Design (VSD) approach offers a practical framework geared towards the addressing of ethical and social issues during design of technological systems. It supports ethical analysis of values, operationalization of values into design, and evaluation of how values are supported and implicated in technological applications. Although VSD is not yet tuned to the specific requirements of nanopharmacy a first exploration provides us with some preliminary keystones. First it shows how issues can be represented by values, how stakeholders related to these values can be involved in the investigation and gives some clues to further conceptual research in the future. Second, it indicates possibilities to integrate VSD into existing medication R&D practises. VSD integration needs to be established with existing testing and development methodologies used in current nanopharmaceutical R&D. The analyses and approach outlined here are all but conclusive; much work still needs to be done. From an ethical perspective, further conceptual investigating of issues and values implicated by nanopharmacy is required, but more importantly, on the empirical and technical

side, further explorations must be implemented on how VSD can be integrating into existing nano-pharmaceutical R&D practise.

References

1. Action Grid (2010) The ACTION-Grid White Paper: Linking Biomedical Informatics, Grid Computing and Nanomedicine, http://www.action-grid.eu/documents/ACTION-Grid%20White%20Paper.pdf, retrieved 1-8-2011
2. Allhoff F, Lin P, Moore M (2010) What is nanotechnology and why does it matter?: From science to ethics. Wiley-Blackwell, Oxford
3. Allhoff F, Lin P (2006) What's so special about nanotechnology and nanoethics? Int J Appl Philos 20(2):179–90
4. Arnall AH (2003) Future technologies, today's choices: nanotechnology, artificial intelligence and robotics; a technical, political and institutional map of emerging technologies, Greenpeace Environmental Trust
5. Bawa R, Johnson S (2009) Emerging Issues in Nanomedicine and Ethics. Nanotechnology & Society, p. 207–223, doi:10.1007/978-1-4020-6209-4_11
6. Bawa R, Melethil S, Simmons WJ, Harris D (2008) Nanopharmaceuticals—patenting issues and FDA regulatory challenges. Am Bar Assoc SciTech Lawyer 5(2):10–15
7. Bawarski WE, Chidlowsky E, Bharali DJ, Mousa SA (2008) Emerging nanopharmaceuticals. Nanomed Nanotech Biol Med 4(4):273–282, Elsevier Inc. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18640076
8. Bennett-Woods D (2008) Nanotechnology: Ethics and society. CRC Press, Boca Raton
9. Brownsword R (2009) Nanoethics: old wine, new bottles? J Consum Policy 32(4):355–379, Springer Netherlands. Retrieved from http://www.springerlink.com/content/f020211848hrk548/?p=8ab7e3b0487c4949a3351d653023c58b&pi=0
10. Califf RM (2004) Defining the balance of risk and benefit in the era of genomics and proteomics. Health Affairs 23 (1):77–87
11. Casci T (2004) Doctor in a cell. Nat Rev Genet 5(6):406. doi:10.1038/nrg1369
12. Cummings ML (2006) Integrating ethics in design through the value-sensitive design approach. Sci Eng Ethics 12:701–715. doi:10.1007/s11948-006-0065-0
13. D'Silva J, Van Calster G (2009) Taking temperature—A review of European Union regulation in nanomedicine. Eur J Health Law 16(3):249–269
14. Eaton MAW (2011) How do we develop nanopharmaceuticals under open innovation? Nanomed Nanotech Biol Med 7(4):371–375
15. Eaton M, Weltring KM (2010) The impact of the open innovation on (Nano-) Healthcare R&D in Europe. For: The European Technology Platform Nanomedicine (ETPN), www.etp-nanomedicine.eu, retrieved 20th August 2011
16. Ebbesen M, Jensen TG (2006) Nanomedicine: techniques, potentials, and ethical implications. In: Journal of Biomedicine and Biotechnology. Volume 2006, Article ID51516, Pages 1–11
17. European Commission (2008) Regulatory Aspects of Nanomaterials. COM (2008) 366, 17.6.2008
18. Scientific committee on emerging and newly identified health risks (Scenihr) (2005). The appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies. Available on line: http://nanobio-raise.org/group/editors/menus/main/activities/view. Retrieved: August 30, 2008
19. European TechnologyPlatform on NanoMedicine (2005) Nanotechnology for Health: Vision paper and and Basis for a Strategic Research Agenda for Nano-Medicine, ftp://ftp.cordis.europa.eu/pub/nanotechnology/docs/nanomedicine_visionpaper.pdf, retrieved 25th of August 2011
20. Davis ME (2009) Design and development of IT-101, a cyclodextrin-containing polymer conjugate of camptothecin. Adv Drug Deliv Rev 61(13):1189–1192, ISSN 0169-409X
21. Friedman B (ed) (1997) Human values and the design of computer technology. Cambridge University Press and CSLI, Stanford University, New York
22. Friedman B, Kahn PH (2000) New directions: A value-sensitive design approach to augmented reality. Proceedings of DARE 2000 on Designing augmented reality environments (pp. 163–164)
23. Friedman B, Kahn PH, Borning A (2002) Value sensitive design: Theory and methods. Engineering, 21(December), 1–8. Department of Computer Science, University of Washington
24. Holm S (2006) Pharmacogenetics, race and global injustice. Dev World Bioethics 8(2):82–88
25. Gabellieri C, Frima H (2011) Nanomedicine in the European Commission policy for nanotechnology, Nanomedicine: Nanotechnology, Biology and Medicine, Available online 28 July 2011, ISSN 1549–9634, doi:10.1016/j.nano.2011.07.003
26. Graur F et al (2011) Ethical Issues in Nanomedicine, MEDITECH 2011. In Vlad S, Ciupa RV (eds), IFMBE Proceedings 36, pp. 9–12, 2011
27. Grunwald A (2010) From speculative nanoethics to explorative philosophy of nanotechnology. NanoEthics 4:91–101, Springer Netherlands. Retrieved from http://www.nanoarchive.org/9602/
28. Guerra G (2008) European Regulatory Issues in Nanomedicine. NanoEthics 2(1):87–97, Retrieved from http://www.springerlink.com/index/10.1007/s11569-008-0031-1
29. Heersmink R, Van den Hoven J, Van Eck NJ, Van den Berg J (2011) Bibliometric mapping of computer and information ethics. Ethics Inform Technol 13(3):241–249
30. Helge K (2009) Emotional intelligence: The possibilities and pitfalls of affective computing software. In AALL Spectrum 14 (Dec. 2009). P 14–17
31. Hongxuan Ren (2004) Attaching great importance to assessment for the safety for nanopharmaceuticals. Available online:

http://www.gsstc.gov.cn/Plan/detail.php?dir=/&n_no=3561. Last available: July1,2008
32. Houdy P, Lahmani M, Marano F (Eds) (2011) Nanoethics and Nanotoxicology. Springer
33. Koepsell D (2011) Innovation and nanotechnology: Converging technologies and the end of intellectual property. Bloomsbury Academic, London
34. Lin P, Allhoff F (2008) Nanoscience and nanoethics: Defining the disciplines. In: Allhoff F, Lin P, Moor J, Weckert J (eds) Nanoethics: The social & ethical implications of nanotechnology. Wiley, Hoboken
35. Maojo V, Martin-Sanchez F, Kulikowski C, Rodriguez-Paton A, Fritts M (2010) Nanoinformatics and DNA-based computing: catalyzing nanomedicine. Pediatr Res 67 (5):481–489
36. McGinn R (2010) Ethical responsibilities of nanotechnology researchers: a short guide. NanoEthics 4(1):1–12
37. Mehta MD (2004) The future of nanomedicine looks promising, but only if we learn from the past. In: Health Law Review, Vol. 13 Nbr. 1, December 2004
38. Miller J (2003) Beyond biotechnology: FDA regulation on nanomedicine. Columbia Sci Technol Law Rev 2002-2003:4
39. Miller S, Selgelid M (2006) Ethical and philosophical consideration of the dual-use dilemma in the biological sciences. Centre for Applied Philosophy and Public Ethics (An Australian Research Council funded Special Research Centre), Australian National University and Charles Sturt University, Canberra
40. Mills K, Fledderman C (2005) Getting the best from nanotechnology: approaching social and ethical implications openly and proactively. IEEE Technol Soc Mag 24 (4):18–26
41. Mol A (2006) Proving or improving: on health care research as a form of self-reflection. Qualitative health research, 16
42. Mol A (2008) The logic of care: Health and the problem of patient choice. Routledge, London
43. Netzer C, Biller-Andorno N (2004) Pharmacogenetic testing, informed consent and the problem of secondary information. Bioethics 18(4):344–360
44. Pison U, Welte T, Giersig M, Groneberg DA (2006) Nanomedicine for respiratory diseases. Springer, European Journal of Pharmacology
45. Duquet D, Trottier E (2006) Ethics and nanotechnology: A basis for action. Commission de l'éthique de la science et de la technologie, Québec, Québec (Province)
46. Sheetz T, Vidal J, Pearson TD, Lozano K (2005) Nanotechnology: Awareness and societal concerns. Technology in Society 27(3):329–345
47. Sandberg A, Bostrom N (2006) Converging cognitive enhancements. Ann NY Acad Sci 1093:201–227
48. Spagnolo AG, Daloiso V (2009) Outlining ethical issues in nanotechnologies. Bioethics 23(7):394–402. doi:10.1111/j.1467-8519.2007.00623.x, September 2009. Available at SSRN: http://ssrn.com/abstract=1484038
49. Sparrow R (2007) Revolutionary and familiar, inevitable and precarious: Rhetorical contradictions in enthusiasm for nanotechnology. NanoEthics 1(1)
50. Reynolds C, Picard R (2004) Affective sensors, privacy, and ethical contracts. In CHI '04 Extended Abstracts on Human Factors in Computing Systems (Vienna, Austria, April 24–29, 2004). CHI '04. ACM, New York, NY, 1103–1106
51. Reynolds C, Picard RW (2005) Evaluation of affective computing systems from a dimensional metaethical position, 1st Augmented Cognition Conference, In conjunction with the 11th International Conference on Human-Computer Interaction, July 22–27, 2005, Las Vegas, NV
52. Smart A, Martin P, Parker M (2004) Tailored medicine: whom will it fit? The ethics of patient and disease stratification. Bioethics 18(4):322–342
53. Swierstra T, Boenink M, Walhout B, van Est R (2009) Converging technologies, shifting boundaries. NanoEthics 3(3):213–216, ISSN 1871-4757
54. Timmermans J, Stahl BC, Ikonen V, Bozdag E (2010) The ethics of cloud computing: A conceptual review. Cloud Computing, HCI, & Design: Sustainability and Social Impacts, 2nd IEEE International Conference on Cloud Computing Technology and Science (CloudCom 2010), Indianapolis, USA
55. Van den Hoven MJ, Miller S, Pogge T (2012) The design turn in applied ethics. (Cambridge University Press) (Forthcoming)
56. Van den Hoven MJ (2008) The tangled web of tiny things: privacy implications of nano-electronics. In: Allhoff F, Lin P (eds) Nanotechnology and society: current and emerging ethical issues. Springer, Heidelberg, pp 147–162
57. Van den Hoven MJ, Weckert J (2008) Information technology and moral philosophy. Cambridge University Press
58. Van de Poel IR (2008) How should we do nanoethics? A network approach for discerning ethical issues in nanotechnology. Nanoethics: Ethics for Technologies that Converge at the Nanoscale 2(1):25–38
59. Virdi J (2009) Bridging the knowledge gap: Examining potential limits in nanomedicine, Spontaneous Generations: A Journal for the History and Philosophy of Science; Vol 2, No 1 : Frankenstein in Lilliput: Science at the Nanoscale
60. Weber K (2006) The next step: privacy invasions by biometrics and ICT implants. Ubiquity 2006, November (Nov. 2006), 1–18
61. Weckert J (2006) The control of scientific research: The case of nanotechnology. In: Tavani HT (ed) Ethics, computing, and genomics. Jones and Bartlett, Sudbury
62. Weston AD, Hood L (2004) Systems biology, proteomics, and the future of health care: toward predictive, preventative, and personalized medicine introduction: paradigm changes in health care. J Proteome Res 3:179–196