*The American Journal of Bioethics*, 9(10): 3–11, 2009

ISSN: 1526-5161 print / 1536-0075 online
DOI: 10.1080/15265160902985027

**Target Article**

# The Coming Era of Nanomedicine

**Fritz Allhoff,** Department of Philosophy, Western Michigan University

This essay presents some general background on nanomedicine, particularly focusing on some of the investment that is being made in this emerging field. The bulk of the essay, however, consists of explorations of two areas in which the impacts of nanomedicine are likely to be most significant: diagnostics and medical records and treatment, including surgery and drug delivery. Each discussion includes a survey some of the ethical and social issues that are likely to arise in these applications.

**Keywords:** nanomedicine, nanotechnology, nanoethics

Nanotechnology has been hailed as the "next Industrial Revolution" (National Nanotechnology Initiative 2000) and promises to have substantial impacts on many areas of our lives. Such impacts will be manifest through many of the applications that nanotechnology will enable; these applications will take advantage of features that are only realized through nanoscale manipulations. And, through these technological advances, many ethical and social issues have been raised.[1]

What, though, is nanotechnology? A common definition, and one that is good enough for the purposes of this discussion, comes from the National Nanotechnology Initiative: "nanotechnology is the understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications." This definition suggests two necessary (and jointly sufficient) conditions for nanotechnology. The first is an issue of *scale*: nanotechnology is concerned with things of a certain size. *Nano* (from the Greek *nannos*, meaning a very short man) means one-billionth, in nanotechnology, the relevant billionth is that of 1 meter. Nanometers are the relevant scales for the size of atoms; for example, a hydrogen atom is $7.874 \times 10^{-10}$ feet in diameter, which is an unwieldy scale to use since the same dimension could be describes as approximately 25% of a nanometer. The second issue has to do with that of *novelty*: nanotechnology does not *just* deal with small things, but rather must deal with them in a way that takes advantage of some properties that are manifest *because* of the nanoscale.[2]

Applications of nanotechnology to medicine are already underway and offer tremendous promise; these applications often go under the moniker of 'nanomedicine' or, more generally, 'bionanotechnology'.[3] This essay presents some general background on nanomedicine, particularly focusing on some of the investment that is being made in this emerging field. The bulk of the essay, however, consists of explorations of two areas in which the impacts of nanomedicine are likely to be most significant: first diagnostic and medical records and second treatment, including surgery and drug delivery.[4] Each discussion includes a survey some of the ethical and social issues that are likely to arise in these applications.

## THE RISE OF NANOMEDICINE

Before moving forward, let us start with a simple conceptual worry, which is how to properly delimit the scope of nanomedicine. Other applications of nanotechnology raise ethical issues, but the status of nanomedicine is somewhat different, in at least a couple of ways. First, as presented in subsequent sections, nanomedicine is not always about specific products, as have been considered in some of these other applications. Rather, nanomedicine can be about techniques in ways that have largely not been considered elsewhere. This challenges some of the classifications in the sense that there is not always some specific *thing* that can be looked at and assessed as nanotechnology (or not). This point will become more clear in the remainder of the discussion.

Second, the non-scientific literature on nanomedicine is, at the time of writing, extremely undeveloped. In the research for this article, only a handful of articles even

Acknowledgment: I thank Patrick Lin, Daniel Moore, and three anonymous reviewers for helpful comments on an earlier version of this manuscript.
Address correspondence to Fritz Allhoff, Department of Philosophy, Western Michigan University, Kalamazoo, MI 49008. E-mail: fritz.allhoff@wmich.edu.

1. For discussion of several different areas in which these concerns are manifest, see Allhoff et al. 2007; in press, especially Part III and Allhoff and Lin 2008.
2. For further discussion of this and other definitions of nanotechnology, see Allhoff 2007.
3. See, for example, Vo-Dinh 2007; Niemeyer and Mirkin 2004; Mirkin and Miemeyer 2007.
4. Some of that discussion is adapted from Allhoff 2007.

countenanced nanomedicine's ethical and social dimensions.[5] This is in stark contrast to some of the topics that have received more attention elsewhere: in a nanotechnology context, the developing world, environment, privacy, enhancement and the military have all received more scholarly attention than nanomedicine (Allhoff et al. 2007; in press; Allhoff and Lin 2008).[6] This is peculiar, especially in the cases of enhancement and the military, which are far more speculative and, to some extent, futuristic than nanomedicine. One suggestion as to why this could be the case is that nanomedicine, unlike some of the other applications of nanotechnology, simply does not raise any ethical or social concerns that have not already appeared in other guises. But my view is closer to the claim that *none* of these applications raises any substantively new concerns; they only change the context in which those concerns are realized (Allhoff 2007). This sort of skepticism is not to cast aspersions on the present project, which can be about elucidating those contexts instead of trying to motivate some new theoretical approach altogether. Nevertheless, the asymmetry between ethical discussion of nanomedicine and other applications of nanotechnology bears notice.

One of the few significant contributions to discussion of the ethical issues in medicine comes from Raj Bawa and Summer Johnson (2008). Bawa and Johnson, before moving to particular discussions about nanomedicine, offer some general comments about the pharmaceutical industry that warrant attention, particularly as is relevant for much of the investment that is being made in nanomedicine. Drug companies are always striving to increase the success rate of their products, as well as to decrease research and development (R&D) costs, including time to development. Getting a new drug to market is an extremely daunting task: the economic cost can be as high as $800 million;[7] the time to market is usually 10–15 years; and only one of every 8,000 compounds initially screened for drug development ultimately makes it to final clinical use (Bawa and Johnson 2008, 211). Annual R&D investment by drug companies has climbed from $1 billion in 1975 to $40 billion in 2003, though the number of new drugs approved per year has not increased at all; it has stayed at a relatively constant 20–30 approvals per year (Sussman and Kelly 2003). (New drugs account for only approximately 25% of the approvals, with the other 75% coming from reformulations or combinations of already-approved drugs.) And, due to these high costs, only approximately 30% of new drugs are recovering their R&D costs. International pressures are mounting on US pharmaceutical companies as well, especially with production being increased in low-cost countries like India and China, coupled with the expiration of some American patents (Bawa and Johnson 2007, 212). None of this is to lament the plights of pharmaceutical companies. The biggest ones—e.g., Johnson and Johnson, Pfizer, Bayer, and GlaxoSmithKline—have annual revenues at or close to $50 billion, and all have under $10 billion/year investments in R&D. Even factoring in total expenses, these biggest companies have annual profits of over $10 billion each (MedAdNews 2007). But of course those companies always want to become more profitable, and nanotechnology offers promise in this regard. It is worth quoting Bawa and Johnson (2007) at length:

> Nanotechnology not only offers potential to address [the above] challenging issues but it can also provide significant value to pharma portfolios. Nanotechnology can enhance the drug discovery process via miniaturization, automation, speed and the reliability of assays. It will also result in reducing the cost of drug discovery, design and development and will result in the faster introduction of new cost-effective products to the market. For example, nanotechnology can be applied to current micro-array technologies, exponentially increasing the hit rate for promising compounds that can be screened for each target in the pipeline. Inexpensive and higher throughput DNA sequencers based on nanotechnology can rescue the time for both drug discovery and diagnostics. It is clear that nanotechnology-related advances represent a great opportunity for the drug industry as a whole (212).

As expected, pharmaceutical companies are already investing in nanotechnology. Analysts have predicted that, by 2014 the market for pharmaceutical applications of nanotechnology will be close to $18 billion annually (Hunt 2004); another report indicates that the United States demand for medical products incorporating nanotechnology will increase more than 17% per year to $53 billion in 2011 and $110 billion in 2016 (Freedonia Group, Inc. 2007; Bawa and Johnson 2007, 212).

The worry is that all of this investment and interest in nanotechnology, particularly as is motivated by a race to secure profitable patents, will lead to a neglect of important ethical issues that should be explored. Bawa and Johnson (2007, 212–213) correctly point out that the time for such reflection is not once these technologies come to market, but before R&D even begins. Insofar as the investments are large and growing and, as mentioned above, insofar as the ethical literature on nanomedicine is almost nonexistent, this imperative has already been violated. The principal ethical issues will have to do with safety, especially toxicity: some of these issues have to do with the nanomaterials involved in nanomedicine, which have been poorly studied thus far, particularly as they interact with complex biological organisms. It is quite likely that some of these applications will

5. For example, JSTOR identifies a single article with *nanomedicine* and *ethics* as keywords, and the Philosophers' Index includes two articles. Even relaxing the *ethics* requirement, JSTOR returns five articles on 'nanomedicine' and Philosophers' Index three articles. This is not to deny that the scientific literature on nanomedicine is more substantial, but rather to say that the *non-scientific* literature is quite anemic.

6. Toxicity is an issue related to nanomedicine that has been present in many of these other areas; questions of how to deal with toxic risk, for example, have ethical dimensions. Toxicity figures into the following discussions of diagnostics and treatment, although that particular focus has not been adequately explored elsewhere.

7. See, for example, DiMasi et al. 2003 and Adams and Brantner 2006.

have unwelcome results in their hosts, at least some of which might not be predicted ahead of time.

## DIAGNOSTICS AND MEDICAL RECORDS

Consider the trajectory of some particular health remediation. Effectively, there are two central steps: first, health care professionals have to assess the health of their patients—both through diagnostics and through the use of preexisting medical records—and, second, they have to choose some treatment plan to address the patients' health issues. This is surely an oversimplified view of medicine, particularly as it fails to include any of medicine's social aspects (e.g., interaction with patients). But, for the purposes this article, it will work just fine: figure out what is wrong with the patient, and then fix it. There are all sorts of diagnostic tools available to the medical community, ranging from simple patient interviews and examinations up to more sophisticated imaging tools like computerized tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET). Other diagnostic tools include blood work, DNA analysis, urine analysis, radiographs, and so on. And there are all sorts of ways to gain access to patients' medical histories. Simple patient interviews, while limited, can be effective, and medical records, prepared by other health care professionals, can offer a wealth of salient information. Once the diagnosis has been made, treatment can proceed; whether through, for example, surgery or drugs, to which we will return in the following section.

Starting with diagnostics and deferring medical records for below, many diagnostic techniques are limited, particularly given certain maladies that health care professionals would like to be able to effectively diagnose. Cancer, for example, is one arena in which nanotechnology is likely to have the biggest impact, and this impact will come both in terms of improved diagnostics and improved treatment (National Cancer Institute 2005). Many cancer cells have a protein, epidermal growth factor receptor (EGFR), distributed on the outside of their membranes; non-cancer cells have much less of this protein. By attaching gold nanoparticles to an antibody for EGFR (anti-EGFR), researchers have been able to bind the nanoparticles to the cancer cells (El-Sayed et al. 2006). Once bound, the cancer cells manifest different light scattering and absorption spectra than benign cells (El-Sayed et al. 2005). Pathologists can thereafter use these results to identify malignant cells in biopsy samples.

This is just one example, but it has three noteworthy features: cost, speed, and effectiveness. Given some other traditional diagnostics that have been available, this one offers an improvement in all three regards. And while cancer is a critical health problem that must be addressed, the general approach that this diagnostic uses can be generalized beyond just cancer. To wit, if nanoparticles can differentially bind to something—meaning that they bind more readily to that thing than to everything else—then it will be easier to identify. And improved diagnostics lead to improved treatments, which lead to better health outcomes.

Diagnostically, the concerns with these sorts of applications center around toxicity, particularly when the applications are utilized *in vivo* (as opposed to *in vitro*). Conventional diagnostic mechanisms, however, manifest the same structural features as nanodiagnostics (i.e., applications of nanotechnology to diagnostics); there do not seem to be any substantially new issues raised in this regard. Consider, for example, x-rays, which use electromagnetic radiation to generate images that can be used for medical diagnostics. But radiation, absorbed in large dosages, is carcinogenic, so health care professionals have to be judicious in their application thereof.[8] The radiation outputs for x-rays are reasonably well understood, as are their toxicities in regards to human biology.[9] As when considering treatment options, health care professionals must consider these toxicities, as well as the benefits of this diagnostic mechanism (perhaps as contrasted with other options). Nanodiagnostics admit of a similar deliberative model, even if some of the risks are, at present, less well understood.

Another possibility is "lab-on-a-chip" technologies, which could detect "cells, fluids or even molecules that predict or indicate disease states" (Bawa and Johnson 2007, 218).[10] These devices could also provide real-time monitoring of various biometric indicators, such as blood glucose levels, as might be useful to a diabetic (Bawa and Johnson 2007, 218). Again, the issues could have to do with toxicity, depending on how these chips are deployed. They might be kept inside the body indefinitely or permanently, which could be different from some of the binding diagnostics that, if administered *in vivo*, would ideally leave the body soon thereafter (e.g., if the cancer cells to which they bound were destroyed; see below). Certainly clinical trials will be important, but it could be hard to get the sort of data that would be relevant for long-term effects. For example, perhaps the diagnostics only manifest toxicity some distant years in the future and only after they have been degraded; this information might not even be available for decades.

Depending on how this information is stored and shared, it could give rise to privacy issues: nanosized chips could be implanted into individuals and serve as repositories for medical information, thus enabling quick access by health care professionals.[11] Strictly speaking, this does not seem to be a diagnostic function, but one of medical record keeping. In other words, these chips are "passive" in the

8. Note that one of the pioneers of radioactivity, Marie Curie died from aplastic anemia, which was almost certainly caused by exposure to radiation. Rosalind Franklin, whose work on x-ray crystallography was critical to the discovery of the double helical structure of DNA, contracted ovarian cancer at a relatively young age; again, her work was almost certainly responsible.

9. There have been numerous studies of the effects of the use radiographic technology in diagnostic procedures. For a recent overview of data relating to risk of cancer, see Berrington de Gonzalez and Darby 2004; Kereiakes and Rosenstein 1980; and National Research Council 1990.

10. See also Craighead 2006.

11. For more discussion, see Allhoff et al. in press, chapter 10.

sense that they are merely storing information. In the previous paragraph, however, I characterized chips that, in some sense, are "active"—they could actually determine what is going on in the body and then make that informational available. This distinction is irrelevant ethically insofar as there are privacy issues regardless, but the passive applications are likely to enable more information. In terms of diagnostics then, the focus should probably be on the active applications, but the passive ones, in virtue of their greater informational potential, give rise to greater privacy concerns. However, I think some skepticism is warranted regarding the privacy issue since, in all likelihood, the chips would merely contain some identification number which would allow access to patients' records through some medical database; the chip itself would not actually contain any medical information, so there is no privacy worry. (Even the identification number could require authentication or decryption as further protections and to prevent the possibility of tracking and surveillance.)

But what are these databases and how are they supposed to work? First, the infrastructure does not presently support this sort of data basing. The ideal is supposed to be something like the following: imagine that someone from California happens to be traveling to New York on business, when she falls seriously ill and is rushed, unconscious, to the emergency room. Maybe even, in the rush to get her to the emergency room, her identification is lost. The emergency room staff can simply scan her triceps, plug her identification number into the database and learn who she is, what previous conditions she has, what drugs she is allergic to, and so on. Treatment can then ensue given this access to her history and records. But, of course, no such database exists.[12] Also, several issues exist for its implementation.

First, it would be a huge endeavor and, presumably, very expensive. We would have to think about whether such a project is worthwhile particularly given that, at least in many cases, there are fairly straightforward ways of getting access to the relevant medical information (e.g., by asking the patient or by using identification to contact a relative). To be sure, this will not always work (e.g., with patients who are unconscious and lack relatives and/or identification), but we would have to think about how many cases could not be handled by more conventional means and whether it would be a worthwhile investment of resources to develop this new system. Second, even if the chips themselves did not pose any substantial privacy worries, the database itself might. If all the medical information really went on some sort of national server, then it could be hacked. If it were retained locally, but allowed for remote access (as it would have to), the same worries would apply. Third, even if the privacy issues were mitigated and gave rise to improved outcomes, there could be ethical issues insofar as those outcomes would only be available to citizens of wealthier countries; as with other disparities, questions of distributive justice arise.[13] There are some other aspects of nanomedicine that are promising and probably without any significant ethical worries. For example, "quantum dots have been used as an alternative to conventional dyes as contrast agents due to their high excitability and ability to emit light more brightly and over long periods of time" (Bawa and Johnson 2007, 218).[14] If quantum dots can be used, especially *in vitro*, to allow for more sensitive detection, then this is a useful application. As mentioned previously, *in vivo* uses raise issues about toxicity, but there are certainly benign applications of nanomedicine that should be pursued if they increase diagnostic abilities. These other issues mentioned previously, regarding toxicity and privacy, are quite likely superable, although ethical attention must be paid to how to move forward. (And, as discussed in the first section of this article, it is unlikely that this imperative has yet been recognized.) Having now offered discussion of how nanomedicine could affect diagnostics and medical record keeping, let the discussion now move on to treatment.

## TREATMENT

This section considers how nanomedicine can be used to improve treatment options and proposes to draw a distinction between two different kinds of treatment: surgery and drugs. 'Surgery' comes from the Greek *χειρουργική* and through the Latin *chirurgiae* which is often translated as 'hand work'. Many cardiac techniques, for example, have to be done manually (literally, by hand) in the sense that a surgeon has to physically intervene on the heart of a patient. Some of these techniques can now be performed remotely, automatically, and so on, but the basic unifier is direct intervention on a physical system by a physician or proxy. Surgery can be contrasted with drug treatment meaning that the administration of some pharmacological substance that is prescribed for remediation of some physical ailment; this latter part of the definition is to distinguish drug *treatment* from other uses of drugs (e.g., recreational). Drugs are often less direct than surgery in the sense that their introduction is not (always) localized. For example, a patient may swallow some pills which have downstream physiological effects in his body, but those effects are mediated by more other processes than the effects of surgery would be. Though nothing substantial hangs on this distinction, it is useful for mode of presentation.[15]

12. Interestingly, research for this article did not find anything written on this issue, despite the fact that the media has often characterized these applications of nanotechnology to be revolutionary for medicine. The following discussion is therefore inherently speculative.

13. See, for example, Allhoff et al. in press, chapter 7.

14. See also Alivisatos 2001.

15. It is worth noting that there are probably non-surgical treatments that do not involve drugs: I do not mean to set up a false dichotomy between surgery and drugs. For example, rest might be a treatment for soreness, but it is neither surgical nor drug-related. Nor, though, is it relevant to nanomedicine; for our purposes, the distinction between surgical and drug-related treatments will suffice, without implying that they are exhaustive.

Nanosurgery (i.e., surgical applications of nanotechnology) enables techniques that are more precise and less damaging than traditional ones; let me offer a few examples.[16] First, a Japanese group has performed surgery on living cells using atomic force microscopy with a nanoneedle (6–8 $\mu$m in length and 200–300 nm in diameter) (Obataya et al. 2005). This needle was able to penetrate both cellular and nuclear membranes, and the thinness of the needle prevented fatal damage to those cells. In addition to ultra-precise and safe surgical needles, laser surgery at the nanoscale is also possible: femtosecond near-infrared (NIR) laser pulses can be used to perform surgery on nanoscale structures inside living cells and tissues without damaging them (Tirlapur and König 2003). Because the energy for these pulses is so high, they do not destroy the tissue by heat—as conventional lasers would—but rather vaporize the tissue, preventing necrosis of adjacent tissue (Ebbesen and Jenson 2006, 2). As noted previously, gold nanoparticles can be used for cancer diagnostics insofar as they can be attached to anti-EGFR which would then bind to EGFR; once bound, cancer cells manifest different light scattering and absorption spectra than benign cells, thus leading to diagnostic possibilities. But this technology can be used for cancer treatment as well as diagnostics: since the gold nanoparticles differentially absorb light, laser ablation can then be used to destroy the attached cancer cells without harming adjacent cells.[17]

What these applications have in common is that they allow for direct intervention at the cellular level. While some traditional laser technologies, for example, have allowed for precision, the precision offered by surgery at the nanoscale is unprecedented. It is not just the promise of being able to act on individual cells, but even being able to act *within* cells without damaging them. Contrast some of this precision offered by nanosurgery with some more traditional surgical techniques. Just to take an extreme example, consider lobotomies, especially as were practiced in the first half of the 20th century: these procedures were effectively carried out by inserting ice picks through the patient's eye socket, and the objective was to sever connections to and from the prefrontal cortex in the hopes of treating a wide range of mental disorders. Independently of whatever other ethical concerns attached to lobotomies—which have fallen out of practice since the introduction of anti-psychotics such as chlorpromazine—these procedures could hardly have any degree of precision. Even given the dark history of lobotomies, one of its highlights was the invention of more precise surgical devices; for example, António Egas Moniz's introduction of the leucotome, for which he won the Nobel Prize in 1949. However surgeries are practiced, precision is always important, meaning roughly that surgeons want to be able to access the damaged area of the patient's body without simultaneously compromising anything not damaged. The gains in precision from ice picks to nanosurgery are multiple orders of magnitude, and even the gains in precision from recent surgical advances to nanosurgery could be a full order of magnitude.

So what are the worries? As alluded to in the first section and will be discussed more in the last, the principal worry is that these surgical techniques carry risks, and that, in the excitement to rush them to market, those risks will not be adequately explored or assessed. For now, though, it is worth noticing that there is nothing special about nanosurgery in this regard: whatever stance we otherwise adopt toward risk is equally transferable to this context. That said, it is not obvious what the risks could be for nanosurgery, though dismissal of potential risks could certainly be one of them. Some of the applications with drug delivery do seem more risky than using high-precision surgical techniques, though I will argue below that those are not endemic to nanomedicine either. Of course there are the generic worries about distributive justice and health care such that only a few might have access to nanosurgical technologies, but those again have nothing in particular to do with nanosurgery.

But let me say something about the use of nanoparticles; as discussed above, these might play a role in various cancer treatments. Of particular concern is the toxicity from nanoparticles that might be used, as well as other safety concerns. Whatever is to be said about these risks, though, it hardly follows that similar concerns do not attach to more traditional approaches. Consider, for example, chemotherapy, which uses cytotoxic drugs to treat cancer. The downside of chemotherapy is that these drugs are toxic to benign cells as well as to malignant ones, and there are side effects such as immunosuppression, nausea, vomiting, and so on. When physicians are prescribing chemotherapy, they therefore have to think about these risks and whether the risks are justified. But whether the treatment option involves nanoparticles or not, this basic calculus is unchanged: physicians must choose the treatment option that offers the best prognosis. Toxicity or side effects count against these outcomes, and improved health counts in favor of them. Obviously, there are epistemic obstacles to such forecasting, and physicians must be apprised of the relevant toxicity and side effect data, but there is nothing unique to nanomedicine in this regard.[18]

The point that I want to make is that there are *already* risks in treatments and there is no good reason to think that the risks of nanosurgery are any higher than the risks characteristic of conventional medicine. In fact, there are good reasons to think that the risks of nanosurgery are actually lower and that the benefits are higher. For example, compare laser ablation of malignant cells to chemotherapy.

16. See also Ebbesen and Jensen 2006.

17. Some commentators talk about those applications for cancer treatment under the aegis of drug delivery but this does not sound quite right: it is not the drug that is being bound to the cancer cells, but rather a nanoparticle that is thereafter used to absorb light, heat the cancer cell, and destroy it. For this reason, I classify it as a surgical tool.

18. As mentioned previously, lack of information about risks is more of an issue in nanomedicine than in some more traditional forms of medicine, although this does not affect general, formal deliberative models.

Chemotherapy, as mentioned previously, is a hard process and one with a lot of costs to the patient (including physical and psychological). If nanomedicine allows us, unlike chemotherapy, to destroy the malignant cells without harming the rest of the organism, it is a definite improvement. Are the nanoparticles that would be utilized toxic? Do they pass out of the body after the treatment? Even supposing that the answers are yes and no, respectively, it is quite probable that these new treatments would be improvements over the old. That is not to say that due diligence is not required, but I suspect that there will not be that much to fear, at least at the appropriate comparative level.

Turning now to drug delivery, there are myriad advantages that nanomedicine will be able to confer. Per the discussion in the first section of this article, there is already a tremendous interest from the pharmaceutical companies in terms of incorporating nanotechnology into their product lines, and that interest is the primary driving force in the rise of nanomedicine; this is not to say that the previously discussed nanosurgical techniques are not impressive, just that they are probably not as profitable. Let me go through three traditional challenges in drug delivery, and explain how nanotechnology can mitigate them.

First, consider absorption of drugs: when drugs are released into the body, they need to be absorbed as opposed to passed through. Nanotechnology can facilitate a reduction in the size of drugs (or at least their delivery mechanisms) and, therefore, an increase in their surface-to-volume ratios. The basic idea here is that it is the surfaces of materials that are most reactive and that, by increasing surface-to-volume ratios, greater reactivity is achieved. As the body absorbs drugs, it has to act on the surfaces of those drugs and, by having more surface area per unit volume, the drugs can be dissolved faster, or even be rendered soluble at all. Speed of absorption is of critical importance to the success of drugs, and nanotechnology will make a difference in this regard. (Also, it is worth noting that nanomedicine may obviate the need for oral administration of drugs in some cases and allow for topical administration: because the drugs will be smaller, they will be more readily absorbed transdermally. Insofar as some patients would prefer this method of administration, it offers another advantage.)

Second, it is not always the case that fast absorption is ideal since, in some cases, it would be better if the drug were released slowly over time. Consider, for example, time-release vitamins: because vitamins B and C are water soluble, they quickly flush from the body if not administered in some time-release manner. If the options were taking a vitamin every couple of hours or else taking one that is slowly released over a longer period of time, there are obvious advantages to the latter. Nanotechnology could be used to create better time-release capacities insofar as it could allow for smaller apertures through which the pharmacological molecules would dissipate. In other words, nanotechnology could help to create lattices with openings through which, for example, single molecules would pass. If only single molecules could pass at any given time from the delivery system (e.g., the capsule), then it would take a longer time to disperse the drug supply and, depending on the application, this could lead to more effective treatment.

Third, because nanotechnology will be able to engineer smaller drugs, the associative drugs might be able to traverse various membranes or other biological barriers that had previously restricted their usefulness. For example, consider the blood–brain barrier, which is a membrane that restricts the passage of various chemical substances (and other microscopic entities, like bacteria) from the bloodstream into the neural tissue. Nanoparticles are able to pass this barrier, thus opening up new possibilities for treatment of psychiatric disorders, brain injuries, or even the administration of neural anesthetic (Nanotechnology to Revolutionize Drug Delivery 2005). In this case, nanomedicine is not just improving existing treatment options, but also perhaps even creating new ones.

Again tabling issues of distributive justice, the principal concern with bringing nanotechnology to bear on drug delivery has to do with toxicity and other risks: we simply do not know how these technologies will interact with the body, and there could be negative consequences. As with the discussion of nanosurgery, this author is inclined to think that the benefits conferred by the application of nanotechnology to drug delivery outweigh the risks, though the risks in drug delivery are probably greater than the risks with nanosurgery. It is worth reiterating, though, that risks pertaining to delivery are not unique to nanomedicine. Consider, for example, the celebrated case of Jesse Gelsinger, who died in a gene therapy trial (Philipkowski 1999). Gelsinger had ornithine transcarbamylase deficiency: he lacked a gene that would allow him to break down ammonia (a natural byproduct of protein metabolism). An attempt to deliver this gene through adenoviruses was made, and Gelsinger suffered an immunoreaction that led to multiple organ failure and brain death. Whether talking about vectors for genetic interventions or nanoparticles, we surely have to think carefully about toxicity, immunoreactions, and other safety concerns; the point is merely that these issues are not unique to nanomedicine.

## MOVING FORWARD

In this last section, let me tie together various themes that have been developed in the preceeding three and, in particular, make some comments about the future of nanomedicine. Throughout, the discussion indicated skepticism about whether nanomedicine raises any new ethical or social issues, or at least ones that have not already been manifest with existing technologies. This skepticism applies to various other areas of nanoethics as well, though perhaps more so to medicine. Issues in privacy might, for example, be transformed by the proliferation of radio frequency

identification (RFID), although I doubt it.[19] But the issues with nanomedicine seem to be, at most, risks (e.g., toxicity and safety) and distributive justice, and in fairly standard ways. Of course these considerations ought to be taken into account, but they should always be taken into account and nothing inherent to nanomedicine makes us think differently about them.

What does make nanomedicine interesting, at least from an ethical perspective, is its extreme profitability. As mentioned in the first section, pharmaceutical companies make tens of billions a dollar on year in profits, and this leads to a different motivational scheme than exists in other applications of nanotechnology. For example, consider nanotechnology and the developing world. The developing world, practically by definition, simply does not have tremendous amounts of money. Staying with pharmaceuticals, a primary ethical concern is that drugs critical for health in the developing world just are not developed because they would not be profitable; consider, for example, the billions of dollars spent in the United States on erectile dysfunction drugs as against the lack of investment for lifesaving anti-malarial medication. This is not to say that the developing world cannot be made profitable,[20] but it has a long way to go to rival domestic profitability.

Applications of nanotechnology to RFID tags raise privacy worries, particularly given the profitability of the RFID industry and the expected proliferation of its products. Wal-Mart, for example, has mandated that its principal suppliers use RFID tags on their deliveries in order to facilitate more effective inventorying.[21] Under a reasonable estimate of a billion tags a year, the revenues would be $50 million annually at $0.05/tag. If Walmart only used 1% of the produced tags, the annual *revenue* for the entire RFID industry (on tags) would be $5 billion, which is about half the annual *profit* of single, large pharmaceutical company. There are other economic impacts of RFID technology, including scanners, manufacturing, training, for example, but, even aggregated, these have to fall well short of the economic impacts of nanomedicine.

Other oft-discussed applications of nanotechnology are probably even less profitable still: consider the environment, human enhancement,[22] and the military.[23] It is always hard to make the environment profitable, particularly since it is more often governments than consumers or industry that have to produce the capital outlay. There will be profit in repairing or protecting the environment, but it will be of a far lesser scale than that available to pharmaceutical companies through investment in nanomedicine. Enhancement will only be available to some people, and some of the widespread availability that the nanomedia has prognosticated warrants serious skepticism. At least in the United States, nearly everyone will take some pharmacological product at some stage of life, and many (or most) of those will be transformed by nanomedicine. Therefore, the scope and, again, profitability are very high for nanomedicine. Finally, consider the military, which is a little more tricky. The Department of Defense (2008), for example, had a 2008 budget of $481 billion, but it is hard to get a sense for what implications this has for sellers of nanotechnology. Obviously the latest war in Iraq plays a large role in this expenditure, as do overall personnel. Will government military contractors be as motivated to pursue nanotechnology as pharmaceutical companies? Or to put it a different way, will nanotechnology have a bigger economic impact on the military than on medicine? This author suspects not, but will not pursue that suspicion here.

Regardless, the point is merely that nanomedicine is likely to be one of the most—if not *the* most—profitable application of nanotechnology and, furthermore, one that is going to be primarily pursued by pharmaceutical companies committed to making profits. These features give rise to ethical concerns insofar as they are harbingers for market-first, ethics-last mantras. Imagine that Johnson and Johnson is competing with Pfizer to bring out the next greatest drug; with a multi-year patent and billions of dollars hanging in the balance. There is a lot of pressure to be first. And, potentially, a lot to be gained by cutting corners along the way, whether during pharmacological development, clinical trials, complete disclosure, or whatever. Organizations like the United States Food and Drug Administration will have to be extremely vigilant but, of course, they always have to be vigilant. The profits are there to be had whether the drugs incorporate nanotechnology or not so, in that sense, this is nothing new. The only point is that these pressures are likely to be more significant in nanomedicine than many or all other applications of nanotechnology.

Moving forward, we must develop an engagement between nanomedicine's promise and its ethical and social implications. In the first section, I pointed out that there has been very little academic or public work done on these issues; at the time of writing, not more than a couple of articles.[24] Surely this needs to be remedied.

19. See Allhoff et al. in press, chapter 10. An RFID tag communicates a unique identification number to an electronic reader by radio waves, thus abrogating the need for either physical contact with the tag (e.g., such as would be necessary to read a bar code), or even a direct line of sight to the tag. These tags have a small microchip, as well as a radio antenna which can transmit data from the chip to the reader. This reader also contains an antenna, as well as a demodulator which can transform the analog radio signal into digital data that can then be used by a computer. Privacy advocates worry that these signals and data can be used for tracking and surveillance.

20. The Health Impact Fund, for example, seeks to incentivize private pharmaceutical companies to invest in global public health. See Hollis and Pogge 2008.

21. RFID-enabled inventory allows that line of sight would not be required (e.g., scannable bar codes) and furthermore, that inventory could be done remotely.

22. Lin and Allhoff 2008.

23. Altman 2006; Moore 2007.

24. A notable exception to this, particularly in terms of public engagement, is noted in European Working Group on Ethics and Science and New Technologies to the European Commission 2007. An abridged version is published in Allhoff and Lin 2008, 187–206.

To have the pharmaceutical companies developing products without an existing forum to discuss the potential effects of those products—including toxicity and other risks—is not good. Again, some of those effects might not be manifest for many years as we simply do not have long-term research about how nanotechnology interacts with the body. The promise is certainly high, but it should be negotiated clearly and carefully with attention to ethical and social implications and an accompanying discourse. ■

## REFERENCES


Adams, C. P., and V. V. Brantner. 2006. Estimating the cost of the new drug development: Is it really $802 million? *Health Affairs* 25(2): 420−428.

Alivisatos, A. P. 2001. Less is more in medicine. *Scientific American* 285(3): 66−73.

Allhoff, F. 2007. On the autonomy and justification of nanoethics. *Nanoethics: The Ethics of Technologies That Converge at the Nanoscale* 1(3): 185−210.

Allhoff, F., et al., eds. 2007. *Nanoethics: The Ethical and Social Dimension of Nanotechnology*. Hoboken, NJ: John Wiley & Sons.

Allhoff, F., and P. Lin. eds. 2008. *Nanotechnology & Society: Current and Emerging Ethical Issues*. Dordrecht, The Netherlands: Springer.

Allhoff, F., et al. *What Is Nanotechnology and Why Does It Matter: From Science to Ethics*. Oxford, UK: Blackwell Publishing. In press.

Altman, J. 2006. *Military Nanotechnology: New Technology and Arms Control*. London, UK: Routledge.

Bawa, R., and S. Johnson. 2008. Emerging issues in nanomedicine and ethics. In *Nanotechnology & Society: Current and Emerging Ethical Issues*. F. Allhoff, and P. Lin, eds. Dordrecht, The Netherlands: Springer, 207−223.

Berrington de Gonzalez, A., and S. Darby. 2004. Risk of cancer from diagnostic x-rays: Estimates for the United Kingdom and 14 other countries. *Lancet* 363(906): 345.

Craighead, H. G. 2006. Future lab-on-a-chip technologies for interrogating individual molecules. *Nature* 442: 387−393.

Department of Defense, Office of Management and Budget. 2008. Available at http://www.whitehouse.gov/omb/budget/fy2008/defense.html (accessed August 29, 2008).

DiMasi, J. A., et al. 2003. The price of innovation: New estimates of drug development costs. *Journal of Health Economics* 22: 151−185.

Ebbesen, M., and T. G. Jensen. 2006. Nanomedicine: Techniques, potentials, and ethical implications. *Journal of Biomedicine and Biotechnology* 2006: 1−11.

El-Sayed, I., et al. 2005. Surface plasmon resonance scattering and absorption of anti-EGFR antibody conjugated gold nanoparticles in cancer diagnostics: Applications in oral cancer. *Nano Letter* 5(5): 829−834.

El-Sayed, I., et al. 2006. Selective laser photo-thermal therapy of epithelial carcinoma using anti-EFGR antibody conjugated gold nanoparticles. *Cancer Letters* 239(1): 129−135.

European Working Group on Ethics and Science and New Technologies to the European Commission. January 17, 2007. Opinion on the ethical aspects of nanomedicine. *Opinion 21.* Brussels, UK: European Commission.

Freedonia Group, Inc. 2007. *Nanotechnology in Healthcare*. Cleveland, OH: Freedonia. Available at http://www.freedoniagroup.com/brochure/21xx/2168smwe.pdf (accessed October 16, 2008).

Freitas, Jr., R. A. 2007. Personal choice in the coming era of nanomedicine. In *Nanoethics: The Ethical Implications of Nanotechnology*. Allhoff, F. et al., eds. Hoboken, NJ: John Wiley & Sons, 161−172.

Hollis, A., and T. Pogge. 2008. *The Health Impact Fund: Making New Medicines Accessible for All (Incentives for Global Health)*. Available at http://www.yale.edu/macmillan/igh/ (accessed January 28, 2009).

Hunt, W. H. 2004. Nanomaterials: Nomenclature, novelty, and necessity. *Journal of Materials* 56: 13−19.

Kereiakes, J. G., and M. Rosenstein. 1980. *Handbook of Radiation Doses in Nuclear Medicine and Diagnostic X-Ray*. Boca Raton, FL: CRC Press.

Lin, P., and F. Allhoff. 2008. Untangling the debate: The ethics of human enhancement. *Nanoethics: The Ethics of Technologies That Converge at the Nanoscale* 2(3): 251–264.

MedAdNews. 2007. The top 50 pharmaceutical companies charts & lists. *MedAdNews* 13(9):

Moore, D. 2007. Nanotechnology and the military. In *Nanoethics: The Ethical and Social Dimension of Nanotechnology*. Allhoff, F. et al., eds. Hoboken, NJ: John Wiley & Sons, 267−275.

Nanotechnology to Revolutionize Drug Delivery. 2005. *Pharma Technologist* March 7, 2005. Available at http://www.in-pharmatechnologist.com/Materials-Formulation/Nanotechnology-to-revolutionise-drug-delivery (accessed August 27, 2008).

National Cancer Institute. 2005. Targeted gold nanoparticles detect oral cancer cells. *Nanotech News.* Available at http://nano.ancer.gov/news_center/nanotech_news_2005-04-25b.asp (accessed August 7, 2007).

National Nanotechnology Initiative: Leading to the Next Industrial Revolution. February 2000. *National Science and Technology Council's Committee on Technology*. Available at http://clinton4.nara.gov/media/pdf/nni.pdf (accessed November 5, 2008).

National Research Council. 1990. *Health Effects of Exposure to Low Levels of Ionizing Radiation*. Washington, DC: National Academics Press.

Niemeyer, C. M., and C. A. Mirkin. 2004. *Nanobiotechnology: Concepts, Applications, and Perspectives*. Weinheim, Germany: Wiley-VCH.

Niemeyer, C. M., and C. A. Mirkin. 2007. *Nanobiotechnology II: More Concepts and Applications*. Weinheim, Germany: Wiley-VCH.

Obataya, I., et al. 2005. Nanoscale operation of a living cell using an atomic force microscope with a nanoneedle. *Nano Letters* 5(1): 27−30.

Philipkowski, K. 1999. Another change for gene therapy. *Wired* October 1, 1999. Available at http://www.wired.com/science/discoveries/news/1999/10/31613 (accessed August 16, 2007).

Sussman, N. L., and J. H. Kelly. 2003. Saving time and money in drug discovery: A pre-emptive approach. In *Business Briefings: Future Drug Discovery 2003*, London, UK: Business Briefings, Ltd.

Tirlapur, U. K., and K. König. 2003. Femptosecond near-infrared laser pulses as a versatile non-invasive tool for intra-tissue nanoprocessing in plants without compromising viability. *The Plant Journal* 31(2): 365–374.

Vo-Dinh, T. 2007. *Nanotechnology in Biology and Medicine: Methods, Devices, and Applications*. Boca Raton, FL: CRC Press.

National Nanotechnology Initiative. *What is Nanotechnology?* Available at http://www.nano.gov/html/facts/whatIsNano.html (accessed July 16, 2007).