

# Nanotechnology and the Ethical Conduct of Research Involving Human Subjects

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## **I. Introduction**

The purpose of Canada's *Tri-Council Policy Statement on the Ethical Conduct for Research Involving Humans*<sup>1</sup> is to promote only research that is conducted according to the highest ethical standards. As a condition of federal funding, researchers who are granted federal funding or who work within institutions that receive federal funding must comply with the ethical principles espoused in the articles of the TCPS. The TCPS is not law nor is it a set of rigid rules. Rather, it is an ethical framework that is intended to provide guidance to researchers and the research ethics boards charged with ethical review of human subject research. "[T]he key is sensitive and thoughtful implementation of the spirit and requirements of the document,"<sup>2</sup> not blind adherence to rules. From the outset, it was recognized that "considerations around the ethical conduct of human subjects are complex and continually evolving" and that ethical principles must be re-evaluated and adapted to the context in which they are applied. As the scope of nanotechnology has inevitably grown to include human subject research, this paper is intended to initiate discussion about the potential impact that it may have on human subject research and to determine whether or how this impact might best be reflected in the TCPS.

Respect for human dignity demands that research be done with a view to morally acceptable ends and that morally acceptable means be used to achieve those ends. Import-

tantly, to be considered ethical, research must also have scientific merit.<sup>3</sup> It is clear that the welfare and integrity of the individual is the paramount consideration in research that is ethical from the perspective of the TCPS. Steps must therefore be taken to ensure that individual research subjects are not instrumentalized either during research or as a result of human subject research.

Additionally, a number of trans-disciplinary guiding ethical principles have emerged that express common standards, values and aspirations of researchers. These principles include:

- Respect for free and informed consent
- Respect for vulnerable persons
- Respect for privacy and confidentiality
- Respect for justice and inclusiveness
- Balancing harms and benefits
- Minimizing harm
- Maximizing benefit

In light of these principles, it is important to consider whether there is anything unique about nanotechnology that will impact the application of these ethical principles. To answer this question and to understand the emerging issues it is important to first define what nanotechnology is and, second, to identify specific areas of research where we can reasonably expect nanotechnology to be used in human subjects.



## II. Technology Overview

### **What is Nanotechnology and how will it be used in Human Subject Research?**

Nanoscale science and engineering is a dynamic domain of science and technology at the confluence of the physics, chemistry, biology, information technology, biotechnology and medicine. “Nanoscience” is the study of the first level of organization of matter (either biological or man-made) that determines its fundamental characteristics and function. It has been described as “the builder’s final frontier.”<sup>4</sup>

Within the nano domain, fundamental characteristics of materials that we typically presume immutable — including electrical conductivity, colour, strength, and melting point can all change. By understanding the altered characteristics of materials at the nanoscale and by tailoring the structure of materials in specific ways it is possible to engineer novel materials with characteristics that are unanticipated from macro-scale observation and measurement. By studying the common features of nanoscale entities like nanocrystals and nanotubes scientists are gaining new insight into natural processes that occur in living systems and in the environment.

“Nanotechnology” is inherently hard to define. The term represents a series of technologies used independently or in combination to make products, perform tasks and to gain a better understanding of science. Canada’s National Research Council describes nanotechnology as:

[M]anufacturing at the molecular level – building things from molecular or nano-scale components. A nanometer is one billionth of a metre (3-4 atoms wide). Nanotechnology proposes the construction of novel nano-scale devices possessing extraordinary properties. Through the development of such instruments and techniques it is becoming possible to study and manipulate individual atoms. This ability is almost in the grasp of humankind.<sup>5</sup>

Through this newfound control over the natural world, nanoscience and the technologies derived from it are expected to have profound societal effects – both positive and negative. It is predicted that:

Few industries will escape the influence of nanotechnology. Faster computers, advanced

pharmaceuticals, controlled drug delivery, biocompatible materials, nerve and tissue repair, surface coatings, better skin care and protection, catalysts, sensors, telecommunications, magnetic materials and devices – these are just some areas where nanotechnology will have a major impact. Indeed, there is a growing appreciation that it is difficult to find areas of manufacturing and industry where nanoscience and nanotechnology will not have an impact.<sup>6</sup>

It has been postulated that “[n]anotechnology today is arguably at about the same stage that information technology occupied in the early 1960s, or biotechnology at the beginning of the 1980s.”<sup>7</sup>

Society appears poised to engage a deeply polarized debate over the benefits and risks of nanotechnology.<sup>8</sup> The ETC Group (an action group on Erosion, Technology and Concentration – formerly RAFI), for example, has recommended an immediate moratorium on commercial production of new nanomaterials and the creation of a global process to evaluate the economic, health and environmental implications of nanotechnology.<sup>9</sup> It recommends strict adherence to the precautionary principle, which they advocate as being “a commonsense approach to Atomotechnology”. Oddly, and simultaneously, they recognize that the precautionary principle is neither uniformly defined nor embraced.<sup>10</sup>

Greenpeace takes a less radical approach than the ETC Group.<sup>11</sup> It recognizes that the impact of nanotechnology will be gradual and limited in the short term and argues that a moratorium would likely be both impractical and harmful. It strongly advises industry players to take the issue of public acceptance of nanotechnology seriously. Failure to do so, they warn, may result in a self-imposed moratorium. Commitment to developing sound environmental practices and in performing relevant research to evaluate human safety is urged. This is particularly salient in light of an increasing number of reports in the academic literature and in the popular press that nanoparticles may pose health risks to animals and humans.<sup>12</sup> It has been predicted that failure, by government and industry, to acknowledge the concerns raised by the critics of nanotechnology may lead to a backlash, similar to that experienced in the context of agricultural biotechnology.<sup>13</sup> Early recognition of the political realities, societal concerns, underlying environmental and human safety issues and their potential relevance to human subject research is essential.



Despite the emerging concerns, Canada, like virtually all other developed countries, is committed to building national capacity in the area of nanotechnology.<sup>14</sup> The National Research Council, the province of Alberta and the University of Alberta are combining resources to build a national institute at the University of Alberta.<sup>15</sup> The National Institute for Nanotechnology, though physically located in Alberta, aspires to attract researchers from across Canada and around the world and catapult Canada onto the international nanotechnology stage.

Though nanotechnology is expected to impact most sectors of the economy, it is expected to have a profound impact on health and health related technologies. Given that health and healthcare provision are among Canada's foremost priorities<sup>16</sup>, the government is eager to find and to adopt more cost effective methods of healthcare delivery.<sup>17</sup> To the extent that nanotechnology is perceived able to provide solutions to current healthcare problems, it will inevitably receive high priority from research funding agencies, including the CIHR.<sup>18</sup> In the medical context, nanoscience is expected to facilitate the development of, among other things:

- improved pharmaceutical products;
- implantable materials for tissue repair and replacement;
- implantable devices (including sensing devices, implantable medical devices and sensory aids);
- improved surgical tools;
- improved diagnostic imaging methods; and
- improved genetic testing capabilities.<sup>19</sup>

Each of these applications are described briefly below.

### **Improved pharmaceutical products**

Nanotechnology has the potential to enable a range of new technologies to facilitate the optimized delivery of pharmaceutical products.<sup>20</sup> Special materials, including nanoscale liposomes, polymers, silica and hydroxyapatite are being used to encapsulate drugs and protect them from biological processes in the body. As compared with their microscale counterparts, nanoparticle based encapsulation materials

tend to have improved diffusion and degradation characteristics.<sup>21</sup> On this basis, it is expected that nano-materials will facilitate the delivery of drugs through the blood brain barrier and into the central nervous system. As a result, effective treatments may be developed for Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis and brain tumours. Similarly nano-encapsulation materials may prove effective in the delivery of drugs to the retina of the eye through the blood-retina barrier.

### **Implantable materials for tissue repair and replacement**

Nanotechnology is facilitating the development of novel materials that can be used for human tissue repair and replacement.<sup>22</sup> Novel biocompatible materials can be used to make permanent implants or temporary structures that can be reabsorbed by the body following surgery. For example, bone and dental implants can be made from biocompatible nano-materials characterized by their increased surface area and improved adhesion characteristics. Tissue regeneration scaffolds made from nanomaterials are being developed with a view to growing a variety of complex human organs. In addition, bioresorbable polymers can be used to make surgical sutures and orthopedic fixation devices that are designed to biodegrade at appropriate rates to facilitate bone healing in a variety of circumstances.<sup>23</sup>

It is envisioned that pharmaceutical-infused nanofibre devices may be applied directly to affected tissue during surgery. One possible application is that a mesh device may be infused with antibiotics, painkillers and/or other medications and implanted around the heart muscle during surgery. The objective is to provide optimized pharmaceutical effect at the critical time via a delivery system that is implanted and does not require surgical removal. Similarly, "smart" nanomaterials may be devised to respond to physical changes in the environment. For example, a change in temperature or pH could stimulate a physical or chemical effect mimicking a natural mechanism. Smart materials may include polymers that can mimic muscle contraction or hydrogels that dissolve according to body chemistry to deliver drugs as needed.

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### ***Implantable devices (including sensing devices, implantable medical devices and sensory aids)***

Nanotechnology offers the ability to develop a variety of implantable or wearable sensing technologies and medical devices to facilitate the continuous collection of highly accurate medical information. Microprocessors and miniature devices can be paired with sensors to diagnose disease, transmit information and to administer treatment automatically (and remotely) if required. Implantable sensors can be used to detect a vast array of chemical or physical properties. For example, sub-dermal sensor microchips are being developed to continuously monitor and transmit data including, heart rate, body temperature and glucose level. Microsensors are also being developed to monitor success or failure of surgical procedures through the real-time assessment of post surgical tissue circulation. Implantable microelectromechanical (MEMS) devices<sup>24</sup> to measure flow rate and acceleration may be used to assess and optimize treatment for individuals suffering from paralysis.

Implantable sensors can be engineered to work with medical devices to automatically administer treatments for a variety of conditions. Implantable microfluidic systems are being developed to dispense drugs on demand. Initial applications of these systems will likely include delivery of chemotherapy drugs for oncology patients and the delivery of drug treatments for patients suffering from a variety of diseases including, autoimmune disorders, HIV/AIDS and diabetes. Implantable sensors that monitor heart rate can also act as a defibrillator to regulate irregular rhythms. Technology used in implantable devices designed to improve visual or aural perception is currently workable at the microscale. These technologies will, in all likelihood, be further miniaturized to the nanoscale. Work is being done to develop retinal implants to restore vision by electronically stimulating functional neurons in the retina. Cochlear implants are being developed to offer individuals with hearing loss devices that will be more precise and that will offer much better sound quality than devices currently available.

### ***Improved surgical tools***

It is anticipated that nanotechnology will inspire an array of improved surgical tools that will allow surgeons to operate on human subjects with greater precision and safety and to monitor patients more accurately. Nanotechnology is being used in the development of smart instruments and surgical robotics for use in laparoscopic or “minimally invasive” surgical procedures. Smart instruments can be made with an ability to interpret the in-vivo surgical terrain and assist the

surgeon in performing surgical procedures. Robotic systems are already being used to give surgeons remote control over highly precise instruments that are inserted into laparoscopic ports in the patient. Specifically, surgical robotics systems are suited for use in gall bladder, prostate, colorectal, gynecological, esophageal, gastric and lung surgeries.<sup>25</sup>

### ***Medical imaging***

Nanotechnology is also spawning a new wave of innovation in the area of medical imaging. For example, nanoparticle probes are being developed for use in magnetic resonance imaging (MRI). Magnetic nanoparticles can be simultaneously attached to antibodies that specifically bind to known antigens on cancer cells<sup>26</sup> or other molecules of biological interest (i.e. fibrin<sup>27</sup> and labeled with a dye that can be visualized on MRI images. Following administration of labeled nanoparticles, images can be taken to assess a patient’s tumour burden. Cancer therapy can similarly be specifically targeted to cancer cells in-vivo. Magnetic nanoparticles can also be targeted to proteins or other molecules of biological relevance and used in functional MRI imaging to gain insight into a variety of human disease processes.<sup>28</sup> Radiolabelled carbon nanoparticles have been used for over 15 years to assess lung ventilation in human patients.<sup>29</sup> A variety of miniaturized wireless medical devices are being developed that can provide high quality images that are not possible with traditional imaging devices. Pills are being developed that contain miniature video recording devices.<sup>30</sup> In this way, the entire digestive system can be imaged and assessed for various diseases including malignancies and ulcerations. Researchers are attempting to develop miniature x-ray devices that can be inserted into the human body. One Israeli company, MediRad, is attempting to make carbon nanotubes into a needle shaped cold cathode that would emit electrons for imaging or therapy. The idea is revolutionary in that if developed, could allow doctors to take precision x-rays inside the body or treat localized areas without damaging the surrounding tissue.<sup>31</sup>

### ***Genetic testing methods***

In perhaps the most ethically challenging medical application, nanotechnology has the potential to further revolutionize genetic testing methods. This is particularly relevant given the simultaneous trend away from linkage analysis towards large-scale population genetic research and towards individualized medicine through the use of pharmacogenomics.<sup>32</sup> Standard testing methods require large sample



sizes and long reaction times to amplify the relevant genetic sequence using polymerase chain reaction (PCR). Microfluidic testing methods that are rapid and that can be performed on small biologic samples (for example, a single human cell) are currently being developed.

It is now possible to manufacture and to use microfluidic chips that can perform PCR and reverse transcription of DNA.<sup>33</sup> Of this work, one author notes that this technology “offers a direct route to . . . the possibility of high-throughput sequence analysis in many practical applications.”<sup>34</sup> It is also now possible that, on a single chip, nanolitre volumes can be simultaneously processed to isolate cells, lyse them and purify their DNA or mRNA.<sup>35</sup> Nanofluidic “nanopore sequencers” have been described for the direct reading of the nucleotide sequence of single stranded DNA.<sup>36</sup> It has been suggested that “if DNA can be shuttled through a 10<sup>-9</sup>m hole at a rate of 2 million bases per second, it would take less than 2 hours to sequence an entire genome.”<sup>37</sup> Benefits of miniaturization include decreased volumes of samples and reagents are required, faster reaction times, high throughput and portability of the testing devices.

“Lab-on-a-chip” technology is being developed to facilitate the performance of a variety of tests on a single chip. It entails the combination of nanotechnology and microfluidics to facilitate the integration of mixing, moving, integration, detection and data processing on small portable devices. This combination of arrays and fluidics can be used to optimize the speed, accuracy and utility of genetic testing as well as other types of testing. This technology is expected to be useful in quantifying gene the expression of particular sets of genes that have been found, through array profiling, to be significant in distinguishing specific disease conditions. In time, these technologies are expected to have a profound impact on clinical medicine.

#### **Other Nano-Innovations That May Impact Human Subject Research**

Importantly, it must be noted that in addition to specific medical applications nanotechnology is also facilitating the development of unobtrusive surveillance devices and markedly improved computer storage capacity.<sup>38</sup> These advances

will permit the collection and storage of vast quantities of many types of human subject data for medical research, social sciences research, market research and other — as yet unanticipated — uses. Accordingly, nanotechnology has the potential to profoundly impact the ways that both observational and quantitative research on human subjects is performed, and the way that the data is stored and accessed.

### **III. Emerging Issues**

#### **General Ethical Concerns**

The TCPS aims to elucidate the duties owed to research subjects by researchers, institutions and the Research Ethics Boards (REBs) that are charged with the review of human subject research. The general principles espoused in the document are intended to help researchers and REBs “to scrutinize the contexts and accommodate the needs of specialized research disciplines.”<sup>39</sup> To be considered ethical, research must be capable of answering the scientific questions posed, must be performed in accordance with the applicable laws and regulations and must accord with the ethical principles espoused in the TCPS.

Applications that are enabled by nanotechnology, like all technological applications, have the potential to be used in ethical and unethical ways. Although science at the nano scale is not ethically distinct from science at the macro scale certain issues become more complex and potentially problematic than when the same or similar applications are applied at the micro scale or larger scales.

General ethical concerns that have been raised in association with biomedical nanotech applications include the following:

- Biomedical nanotech applications have the potential to medicalize normal human conditions and further blur the distinction between “health” and “disease”.
- Applications derived from nanotechnology have the potential to further marginalize those in society who are perceived as disabled.

*Society appears poised to engage a deeply polarized debate over the benefits and risks of nanotechnology.*



- Biomedical nanotech applications may be used inappropriately to further human improvement. Nanotechnology may facilitate the development of a variety of devices that will enable the surreptitious collection of human subject data. There are profound privacy and confidentiality issues that arise in light of this possibility.
- Nanotechnology may have the effect of widening the gap between those in the developed world and those in the developing world, despite the emerging ethical imperative that the results of human subject research benefit all of humanity.
- Certain biomedical nanotech applications may confound the conventional boundary between “living” and “non-living”. There are profound conceptual and philosophical implications that arise from this blurring.
- Biomedical applications derived from nanotechnology are likely to be disruptive and are expected to have profound impacts in the area of health service delivery. Which applications will government fund? How will the technology be assessed? Will applications not funded by government be made available for individuals who are willing to pay?
- The development of nanotechnology applications (as with the development of virtually all biotech applications) will depend heavily on private investment therefore compounding ongoing concerns that the TCPS does not apply directly to privately funded research that is performed in the private sector.

*At the policy level, what steps need to be taken to ensure the safe, ethical and timely adoption of the products of nanotechnology?*

For example, there are a number of relevant questions that remain unanswered that relate to a discussion of nanotechnology-enabled genetic, genomic, proteomic and metabolomic analyses. These include:

- Is it possible for human subjects to consent generally to future research involving their biological samples or genetic data derived from their biological samples regardless of the specifics of the research to be performed?
- Can human subjects delegate consent-granting authority to an REB for future research that has scientific merit and is deemed ethical?
- Do REBs have sufficient knowledge and experience in dealing with genetic research and population genetic research to warrant delegation of authority to them by research subjects?

research be applied in the context of population genetic research?

- How will the application of nanotechnology in the area of genetic testing challenge the traditional boundary between the patient-centered autonomy-driven individualistic research ethics and communitarian norms that underpin public health research? How or should the principles underlying public health apply in this context?

### **Law & Regulation**

In addition to the ethical challenges noted above, nanotechnology applications will, in all likelihood, prove challenging from a regulatory perspective. Some of the issues that need to be considered proactively include:

- How will Health Canada and Environment Canada interact to regulate products that implicate nanotechnology?
- How should human safety be most appropriately measured and monitored in this context? Are the existing environmental standards applicable to particulate pollution and norms for pre-clinical and clinical testing of drugs and medical devices appropriate in the context of nanotechnology?

### **Specific Ethical Concerns Relevant in the Context of Genetic Testing**

As nanotechnology has the potential to greatly increase throughput and decrease the cost of genetic testing methodologies, it also has the potential to magnify a number of ethical challenges previously identified in the context of human genetics. Mass testing at low cost coupled with the trend towards large-scale bio-banking and improved bio-informatics capabilities, will inevitably inspire heightened concerns over issues of informed consent, genetic privacy and commercialization.



- At the policy level, what steps need to be taken to ensure the safe, ethical and timely adoption of the products of nanotechnology?
- Are the legal norms governing informed consent in Canada sufficiently adaptable to permit individuals to consent to present and future (as yet undefined) genetic research involving their biologic materials or data derived from their biological samples? How does this vary across provincial jurisdictions? How will nanotechnology challenge the existing federal and provincial privacy laws governing health information?
- How will concerns over gene patenting and the adverse impact of patents on the research environment translate into the realm of nanotechnology?

## Conclusions

Nanotechnology will have a broad impact on biomedical research generally. At present, it is clear that specific biomedical applications in the areas of human genetic research (especially large-scale population genetic research) bio-informatics and pharmacogenomics are being transformed, to one degree or another, by nanotechnology. It is inevitable that, despite our best efforts, nanotechnology will spawn an array of novel innovations that are not presently envisioned. Having said this, it appears that the general principles of the TCPS are applicable and appropriate to human subject research that implicates nanotechnology.

The specific sections of the TCPS that concern free and informed consent (Article 2), privacy and confidentiality (Article 3), human genetic research (Article 8) and human tissue research (Article 10) should be updated to better reflect the ethical and legal uncertainty that has emerged with respect to the norms of population genetic research. In addition, a new section specifically addressing the ethical issues arising at the interface of traditional individualistic, autonomy-driven research ethics and communitarian public health research ethics would help REBs to perform appropriate ethical review of research protocols. In addition, nanotechnology's potential to inspire unobtrusive surveillance devices and their potential use in biomedical and other observational research should be addressed within the TCPS.

In sum, the medical technologies that are described in this paper all fall well within the realm of the real or the possible.

It is only a matter of time before these, and other nanoscience-based innovations are realized. As the example of agricultural biotechnology reveals, any progress towards public acceptance and the legitimate introduction of new technologies in society depends on public engagement and public awareness of the new technologies. Public acceptance strongly depends on trust in government and its agencies to oversee the research and development and marketing phases of the commercial process. The "21st-Century acceptance model" has been described as one in which "technological innovations are received on a voluntary basis where the perceptible usefulness of the new technology products are balanced against associated risks that are shown to be manageable."<sup>40</sup> Human subject research that is scientifically sound, ethical and subject to insightful ongoing review by REBs that are well-equipped to deal with the issues that confront them will go a long way towards ensuring public trust.

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- 1 Medical Research Council, Natural Sciences and Engineering Research Council of Canada & the Social Sciences and Humanities Research Council of Canada, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Human Subjects* (Ottawa: Public Works & Government Services, 1998) [TCPS].
- 2 *Ibid.* at i.1.
- 3 To be ethically sound, biomedical research on human subjects must have scientific merit. This means that the proposed research "is capable of addressing the questions asked". Research Ethics Boards are responsible for ensuring that scientific merit has been assessed prior to ethics approval, see TCPS, Article 1.5.



Prior to human trials, drugs and medical devices require relevant pre-clinical research, including animal research to assess toxicity in an animal species and to predict the safety and efficacy in human subjects. Health Canada's Therapeutic Products Directorate is the Canadian federal authority that regulates pharmaceutical drugs and medical devices for human use. Prior to being given market authorization, a manufacturer must present substantive scientific evidence of a product's safety, efficacy and quality as required by the *Food and Drugs Act*, R.S.C. 1985, c. F-27, and the *Food and Drug Regulations*, C.R.C. 870. The Biologics and Genetic Therapies Directorate is responsible for the regulation of biological and radio-pharmaceutical drugs, including blood and blood products, viral and bacterial vaccines, genetic therapeutic products, tissues, organs and xenografts. This includes evaluating and monitoring their safety, effectiveness and quality.

- 4 National Science and Technology Council Committee on Technology, "Nanotechnology: Shaping the World Atom by Atom", online: World Technology Evaluation Center <[www.wtec.org/Loyola/nano/IWGN.Public.Brochure/](http://www.wtec.org/Loyola/nano/IWGN.Public.Brochure/)> at 1, citing Richard Smalley. Online: National Research Council <[www.nrc-cnrc.gc.ca/nanotech/about\\_e.html](http://www.nrc-cnrc.gc.ca/nanotech/about_e.html)>.
- 5 UK Advisory Group on Nanotechnology, *New Dimensions for Manufacturing: A UK Strategy for Nanotechnology* (London: Department of Trade and Industry, 2002) at 12. See also Harold Brubaker, "Nanotechnology is Hot, if you're into Mundane Products" *smalltimes* (9 April 2004), online: [smalltimes](http://www.smalltimes.com/document_display.cfm?document_id=7701) <[www.smalltimes.com/document\\_display.cfm?document\\_id=7701](http://www.smalltimes.com/document_display.cfm?document_id=7701)>.
- 6 UK Advisory Group on Nanotechnology Applications, *ibid.* at 23.
- 7 See e.g. ETC Group, *From Genomes to Atoms: The Big Down: Atomtech – Technologies Converging at the Nano-scale* (Winnipeg: ETC Group, January, 2003) online: ETC Group <<http://www.etcgroup.org/documents/TheBigDown.pdf>>. The stated goal of this report is to "translate the complex scientific information and to catalyze widespread public debate" (at 6). In conclusion it is the position of the ETC that "[g]iven the concerns raised over nanoparticle contamination in living organisms, governments should declare an immediate moratorium on commercial production of new nanomaterials and launch a transparent global process for evaluating the socio economic, health and environmental applications of the technology"(at 25). See also ETC Group, "No Small Matter

II: The Case for a Global Moratorium" (2003) 7:1 ETC Group Occasional Paper Series, online: ETC Group <[http://www.etcgroup.org/documents/Occ.Paper\\_Nanosafety.pdf](http://www.etcgroup.org/documents/Occ.Paper_Nanosafety.pdf)>.

- 9 ETC Group, "The Big Down" *ibid.* at 72.
- 10 *Ibid.* But see Cass R. Sunstein, "Beyond the Precautionary Principle" Public Law and Legal Theory Working Paper #38, online: Social Science Research Network Electronic Paper Collection <[http://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=307098](http://papers.ssrn.com/sol3/papers.cfm?abstract_id=307098)> at 2. Sunstein criticizes the precautionary principle in its strict form as "impos[ing] a burden of proof on those who create potential risks, and it requires regulation of activities even if it cannot be shown that those activities are likely to produce significant harms." Sunstein rejects this strong form of the precautionary principle because it leads nowhere. In effect, the principle is paralyzing. Rather, he argues that "[t]he salutary moral and political goals of the precautionary principle should be promoted through other, more effective methods."
- 11 Alexander Huw Arnall, *Future Technologies, Today's Choices* (London: Greenpeace Environmental Trust, 2003) at 41.
- 12 See Peter H. Hoet, Abderrahim Nemmar & Benoit Nemery, "Health Impact of Nanomaterials?" (2004) 22 *Nature Biotechnology* 19; Eva Oberdorster, "Manufactured Nanomaterials (Fullerenes, C60) Induce Oxidative Stress in Brain of Juvenile Largemouth Bass", online: EHP <<http://ehp.niehs.nih.gov/members/2004/7021/7021.pdf>>; Alexandra Goho, "Tiny Trouble" *Science News* 165:14 (3 April 2004) 211; Alex Kirby, "Tiny Particles 'Threaten Brain'" *BBC News* (8 January 2004), online: BBC News, UK Edition <<http://news.bbc.co.uk/1/hi/sci/tech/337959.stm>>. But see Vicki Colvin, "The Potential Environmental Impact of Engineered Nanomaterials" (2003) 21 *Nature Biotechnology* 1166; Emmanuelle Schuler, "A Prospective Look at Risk Communication in the Nanotechnology Field" (2004) *Health L. Rev.* [also in this edition].
- 13 A. Mnyusiwalla, A.S. Daar & P.A. Singer, "'Mind the Gap': Science and Ethics in Nanotechnology" (2003) 14 *Nanotechnology* R9; see also G. Pascal Zachary, "Ethics for a Very Small World" (2003) 137 *Foreign Policy* 108.
- 14 See e.g. *Speech From the Throne to Open the Third Session of the Thirty-Seventh Parliament of Canada*, February 2, 2004. It is expressly stated that: "We want a Canada that is a world leader in developing and ap-



- plying the path-breaking technologies of the 21<sup>st</sup> Century – biotechnology, environmental technology, information and communications technologies, health technologies, and nanotechnology.” [Emphasis added].
- 15 See generally “NRC Nanotechnology Institute to be Among the World’s Most Advanced”, online: National Institute for Nanotechnology <[http://nint-innt.nrc-cnrc.gc.ca/newsroom/article4\\_e.html](http://nint-innt.nrc-cnrc.gc.ca/newsroom/article4_e.html)>. The 15,000 m<sup>2</sup> quiet facility will cost \$40M to build. A further \$80M will be spent on equipment, staff and operations. These costs are to be shared by the NRC (\$60M), the Alberta Government and the University of Alberta (\$60M). The Federal government has committed an additional \$12M per year for operating costs commencing in year six. The NRC is committed to providing \$24M per year in infrastructure support. When the relative size of the economy is taken in to consideration, it is estimated that Canada lags in nanotech investment by a factor of 2-3 as compared with the United States.
  - 16 Conference Board of Canada, *Canadians’ Values and Attitudes on Canada’s Health Care System: A Synthesis of Survey Results*, October 2000.
  - 17 Commission on the Future of Health Care in Canada, *Building on Values: The Future of Health Care in Canada* (Ottawa: Commission on the Future of Health Care in Canada, 2002) (Commissioner Roy J. Romanow, Q.C.), online: Health Canada <[www.hcsc.gc.ca/English/pdf/care/romanow\\_e.pdf](http://www.hcsc.gc.ca/English/pdf/care/romanow_e.pdf)>; The Senate Standing Committee on Social Affairs, Science and Technology, *The Health of Canadians – The Federal Role*, vol. 6 (Ottawa: The Committee on Social Affairs, Science and Technology, 2002) (Chair: The Honourable Michael J.L. Kirby), online: Parliament of Canada <<http://www.parl.gc.ca/37/2/parlbus/commbus/senate/com-e/soci-e/rep-e/repoct02vol6-e.htm>>.
  - 18 Canadian Institutes of Health Research, “Regenerative Medicine and Nanomedicine: Innovative Approaches in Health Research”, online: CIHR <[www.cihr.irscc.gc.ca/e/services/16052.shtml](http://www.cihr.irscc.gc.ca/e/services/16052.shtml)>. There is a planned re-launch of this initiative later this year.
  - 19 Neil Gordon & Uri Sagman, “Nanomedicine Taxonomy” Briefing Paper for the CIHR Institute of Neurosciences & Mental Health Addiction, February 2003, online: CIHR <[www.regenerativemedicine.ca/nanomed/Nanomedicine%20Taxonomy%20\(Feb%202003\).PDF](http://www.regenerativemedicine.ca/nanomed/Nanomedicine%20Taxonomy%20(Feb%202003).PDF)>. The subsequent discussion of specific nanomedicine applications draws heavily from this paper.
  - 20 Robert Langer, “Where a Pill Won’t Reach” (2003) 288:4 *Scientific American* 50.
  - 21 Ai Lin Chun *et al.*, “Helical Rosette Nanotubes: A More Effective Orthopaedic Implant Material” (2004) 15 *Nanotechnology* S234.
  - 22 See generally Robert Langer & David A. Tirrell, “Designing Materials for Biology and Medicine” (2004) 428 *Nature* 487.
  - 23 L.G. Griffith, “Polymeric Biomaterials” (2000) 48 *Acta Materialia* 263.
  - 24 MEMS is an acronym for “micro-electromechanical systems”. MEMS technology embeds mechanical devices such as fluid sensors, mirrors, actuators, pressure and temperature sensors, vibration sensors and valves in semiconductor chips. Typical MEMS devices combine sensing, processing and/or actuating functions to alter the way that the physical world is perceived and controlled.
  - 25 See *e.g.* Erika Jonietz, “5 Killer Patents” (2004) 107:4 *Technology Review* 66. In this article, Jonietz highlights five groundbreaking U.S. patents, one of those listed is U.S. patent 6,593,884 which describes a system for visually tracking the locations of bronchoscopes used in lung biopsies.
  - 26 Anil K. Patri *et al.*, “Antibody-dendrimer conjugates for targeted prostate cancer therapy” (2002) 86 *Polymer Materials Science and Engineering* 130.
  - 27 See *e.g.* G. Lanza *et al.*, “Molecular Imaging and Targeted Drug Delivery with a Novel, Ligand-Directed Paramagnetic Nanoparticle Technology” (2002) 9 *Academic Radiology* S330.
  - 28 See *e.g.* P. Winter *et al.*, “Relaxivities of Paramagnetic Nanoparticle Contrast Agents for Targeted Molecular Imaging” (2001) 9 *Proceedings of the International Society of Magnetic Resonance Medicine* 54.
  - 29 See online: Technegas <<http://jcsmr.anu.edu.au/technegas/home.html>>. Regulatory approval for Technegas has been obtained in Canada by Vita Medical Ltd; See also W.M. Burch, P.J. Sullivan & C.J. McLaren, “Technegas – A New Ventilation Agent for Lung Scanning” (1986) 7 *Nuclear Medicine Communications* 865.
  - 30 Capsule Endoscopy is a technique developed by Given Imaging. Their “M2A” is a non-invasive method for direct visualization of the entire small intestine and is described on the Given Imaging website as a “first-line tool in the detection of abnormalities of the small bowel.” The patient ingests a single use



video colour-imaging capsule that travels through the digestive system and is naturally excreted. The patient wears a data recorder that receives signals from the capsule through an array of sensors placed on the patient's body. Individual images are processed into a video that permits physicians to view the intestine. Regulatory approval has been granted by Health Canada for the Given System. See online: Given Imaging <[www.givenimaging.com](http://www.givenimaging.com)>. And see Suthat Liangpunsakul *et al.*, "Wireless Capsule Endoscopy Detects Small Bowel Ulcers in Patients with Normal Results from State of the Art Enteroclysis" (2003) 98 *American Journal of Gastroenterology* 1295.

31 Avi Machlis, "Seeing Nanotube X-ray Through from Idea to Product Proves Hard" *smalltimes* (18 July 2002), online: *smalltimes* <[www.smalltimes.com/document\\_display.cfm?document\\_id=4111](http://www.smalltimes.com/document_display.cfm?document_id=4111)>.

32 See *e.g.* Eliot Marshall, "Preventing Toxicity With a Gene Test" (2003) 302 *Science* 588. See also Nuffield Council on Bioethics, *Pharmacogenetics: Ethical Issues* (London: Nuffield Council on Bioethics, 2003).

- 33 Pierre J. Obeid *et al.*, "Microfabricated Device for DNA and RNA Amplification by Continuous Flow Polymerase Chain Reaction and Reverse Transcription-Polymerase Chain Reaction with Cycle Number Selection" (2003) 75 *Analytical Chemistry* 288.
- 34 Andrew J. deMello, "DNA Amplification Moves On" (2003) 422 *Nature* 28 at 29.
- 35 Jong Wook Hong *et al.*, "A Nanoliter-scale Nucleic Acid Processor with Parallel Architecture" (2004) 22 *Nature Biotechnology* 435.
- 36 Deirdre R. Medrum & Mark D. Holl, "Microscale Bioanalytical Systems" (2002) 297 *Science* 1197.
- 37 *Ibid.* at 1198.
- 38 Michael D. Mehta, "Privacy vs. Surveillance: How to Avoid a Nano-Panoptic Future" *Canadian Chemical News*, 5 (Nov/Dec 2002) 31.
- 39 *Supra* note 1 at i.2.
- 40 *Supra* note 11 at 61.

## Articles for Submission

The *Health Law Review* has a wide audience of subscribers and welcomes articles from the health disciplines, ethics, philosophy, and law. Articles should be submitted by email or on CD. Check our website at [www.law.ualberta.ca/centres/hli](http://www.law.ualberta.ca/centres/hli) for specific information on formatting prior to forwarding your paper.

Endnotes **must** comply with the Canadian Guide to Uniform Legal Citation (5th ed.).

### Deadlines:

October 15, 2004 and February 15, August 15, 2005

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