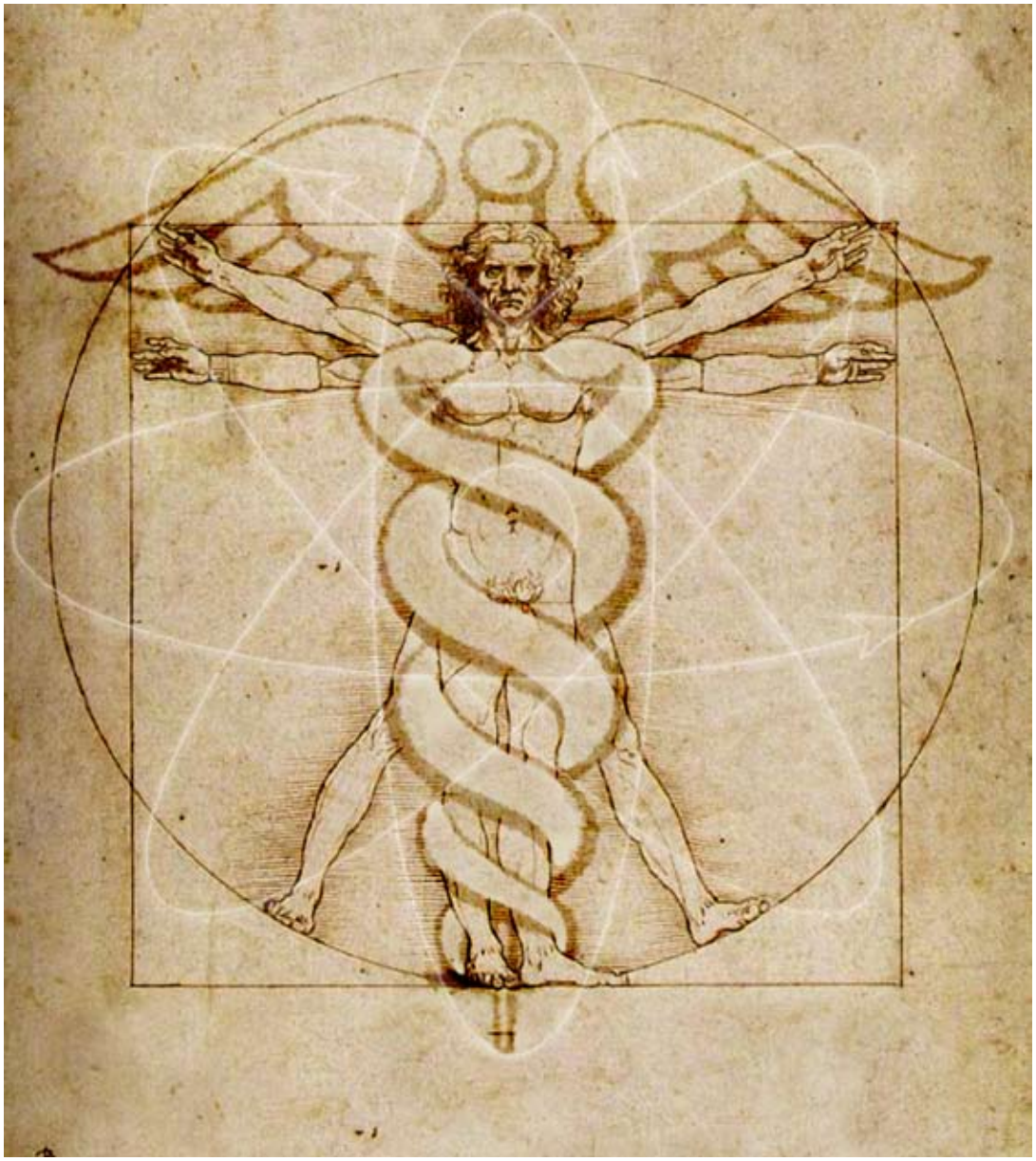

NANOTECH Rx

Medical Applications of Nano-scale Technologies: What Impact on Marginalized Communities?

Nanotech Rx – At a Glance

Issue: Medical applications of nano-scale technologies have the potential to revolutionize healthcare by delivering powerful tools for diagnosing and treating disease at the molecular level. But the current zeal for nano-enabled medicines could divert scarce medical R&D funds away from essential health services and direct resources away from non-medical aspects of community health and wellbeing. Although nanomedicine is being touted as a solution to pressing health needs in the global South, it is being driven from the North and is designed primarily for wealthy markets. Using nano-scale technologies, the pharmaceutical industry's ultimate goal is to make every person a patient and every patient a paying customer by "medicating" social ills with human performance enhancement (HyPE) drugs and devices. Nano-enabled HyPEs could usher in an era of two-tiered humans – *Homo sapiens* and *Homo sapiens 2.0*.

Market: As of mid-2006, 130 nanotech-based drugs and delivery systems and 125 devices or diagnostic tests are in preclinical, clinical or commercial development. The combined market for nano-enabled medicine (drug delivery, therapeutics and diagnostics) will jump from just over $1 billion in 2005 to almost $10 billion in 2010 and the US National Science Foundation predicts that nanotechnology will produce half of the pharmaceutical industry product line by 2015. Nanomedicine will help big pharma extend its exclusive monopoly patents on existing drug compounds and on older, under-performing drugs. Analysts suggest that nanotech-enabled medicine will increase profitability and discourage competition.

Impact: Nanomedicine may have its greatest impact in the realm of "human performance enhancement" (HyPE). Nanomedicine in combination with other new technologies will make it theoretically possible to alter the structure, function and capabilities of human bodies and brains. In the near future, nano-enabled HyPE technologies will erase distinctions between "therapy" and "enhancement" and could change, quite literally, the definition of what it means to be healthy or human.

Reality check: Ironically, crucial questions remain about the health and environmental impacts of nanomaterials that are being used to develop nanomedicines. The nascent field of "nanotoxicology" is awash with uncertainty. Despite the fact that nano-scale products have already been commercialized (including nanomedicines), no government in the world has developed regulations that address basic nano-scale safety issues.

Policy: Can OECD donors who have failed to deliver promised mosquito netting to malaria-stricken countries and who have managed to provide only one condom per adult male per annum to combat HIV/AIDS in the global South really claim that hefty investment in new nanomedicines will pay off for poor countries? Governments urgently need broad, participatory societal and scientific, ethical, cultural, socioeconomic and environmental risk assessment to evaluate nanomedicine. Policies must be guided by the concerns of civil society and social movements, including disability rights and women's organizations. To keep pace with technological change, an intergovernmental framework is needed to monitor and assess the introduction of new technologies. At its next meeting in 2007, the World Health Assembly should undertake a full analysis of nanomedicine within this wider social health context.

NANOTECH Rx

Medical Applications of Nano-scale Technologies: What Impact on Marginalized Communities?

September 2006

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Original artwork by Reymond Pagé.

ETC group is dedicated to the conservation and sustainable advancement of cultural and ecological diversity and human rights. To this end, ETC group supports socially responsible developments of technologies useful to the poor and marginalized and it addresses international governance issues affecting the international community. We also monitor the ownership and control of technologies and the consolidation of corporate power.

ETC Group has produced a series of reports on the social and economic impacts of technologies converging at the nano-scale:

Extreme Genetic Engineering: An Introduction to Synthetic Biology
forthcoming 2006

Nanotech Rx – Medical Applications of Nano-scale Technologies: What Impact on Marginalized Communities?
September 2006

NanoGeoPolitics: ETC Group Surveys the Political Landscape
July/August 2005

Nanotech's Second Nature Patents: Implications for the Global South
June 2005

Down on the Farm: The Impacts of Nano-scale Technologies on Food and Agriculture
November 2004

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Executive Summary

This report examines medical applications of nanotech-enabled drugs, devices and diagnostic tools. What impact will nanomedicine have on the pharmaceutical industry? What role will nano-enabled medicine play in addressing the health needs of marginalized communities, especially in the global South?

Medical applications of nano-scale technologies have the potential to deliver new and powerful tools for detecting, diagnosing and treating disease at the molecular level. Nanotech enthusiasts claim that nano-enabled medicine will revolutionize healthcare.

Developments include, for example:

- Nanosensors circulating inside the body to monitor glucose, hormone or cholesterol levels
- Gold nanoshells that zero in on cancer cells; once identified the tumor cells can be destroyed with a non-invasive laser
- "Smart" nanoparticles that seek out a specific location within the human body and then deliver a precisely targeted drug dose
- Luminescent quantum dots to track a single protein in a living cell
- Silver nanoparticles that kill antibiotic resistant microbes
- Nano-structured, three-dimensional scaffolding to grow new human tissues and organs

Medical applications of nanotechnology may sound like science fiction, but they're not – a handful of nano-enabled drugs and devices are here now – and there's much more coming down tiny tech's pipeline. As of mid-2006, 130 nanotech-based drugs and delivery systems and 125 devices or diagnostic tests have entered preclinical, clinical or commercial development. The combined market for nano-enabled medicine (drug delivery, therapeutics and diagnostics) will jump from just over $1 billion in 2005 to almost $10 billion in 2010. Governments – not corporations – are so far taking the lead in nanomedicine R&D. Publicly-funded researchers and nanobiotech start-up companies are the major players today; big pharma is still on the sidelines – but analysts predict they'll get in the game soon.

While nano-enabled medicine could bring benefits, it is moving forward in the absence of public debate on its far-reaching social and economic impacts. Some nanoproducts that are intended for use in the human body could be therapeutic, but there are many unanswered questions about nanotech's impact on health and the environment. Nanoproducts incorporating engineered nanomaterials could enter the body unintentionally via the environment or the food chain. Developments in nanomedicine could result in healthier people even while novel nanomaterials in the environment could make people sick. No one is sure yet how to distinguish between benign and dangerous nanoproducts and the nascent field of "nanotoxicology" is awash with uncertainty.

Technologies that come together at the nano-scale (including biotechnology, neurotechnology

"Nanotechnology's bag of tricks for inventing new molecules and manipulating those available naturally could be dazzling in its potential to improve health care…nano-technology may enable better early warning systems for cancer and heart disease, cures for progressive diseases like cystic fibrosis, techniques for making implants like artificial hips more successful, and even artificial kidneys."

– Barnaby J. Feder, "Doctors Use Nanotechnology to Improve Health Care," *New York Times*, November 1, 2004.

While nano-enabled medicine could bring benefits, it is moving forward in the absence of public debate on its far-reaching social and economic impacts.

In the near future, nano-tech-enabled technologies intended for use in the body will erase any remaining distinction between "therapy" and "enhancement" and could change, quite literally, the definition of what it means to be human.

Industry analysts are already predicting that nanomedicine will increase profitability, expand a firm's intellectual property estate and discourage competition.

and information technologies) will go far beyond tiny drug delivery devices and cell-level diagnostics for sick people. Technological convergence will make it theoretically possible to alter the structure, function and capabilities of human bodies and brains. In the near future, nanotech-enabled technologies intended for use in the body will erase any remaining distinction between "therapy" and "enhancement" and could change, quite literally, the definition of what it means to be human. Some people claim that nanotech will help to extend human life span well beyond a century (i.e., "eliminate premature death") and allow us to upload information directly to our brains. Ultimately, the broad acceptance of human performance enhancement technologies (HyPEs) – assuming they function as designed – will create a new "ability divide" between those who can afford to buy them and those who cannot (or those who choose to resist them).

Nano-scale technologies have been touted as techno-tools for helping to achieve the Millennium Development Goals, the United Nations' targets for promoting human development and encouraging social and economic sustainability in the global South.[1] However, innovations in nanomedicine are currently being driven from the North and are designed primarily for OECD markets. Nanotech-enabled drugs and devices will play a role in securing and extending exclusive monopoly patents on existing drug compounds and older, under-performing drugs. Industry analysts are already predicting that nanomedicine will increase profitability, expand a firm's intellectual property estate and discourage competition.[2] Under this business-as-usual scenario, nanotech's medical innovations are likely to further concentrate the power of the pharmaceutical industry and have little relevance for addressing health and poverty in marginalized communities.

The development of nano-enabled medicine and its potential to address global health needs must be examined in a larger social and political context. The global health crisis does not stem from a lack of innovation or medical technology. Despite decades of dazzling advances in life-saving and life-extending technologies, one third of the world's population lacks regular access to essential medicines.[3] In parts of Africa and Asia, this figure rises to more than half the population. According to reports published by the World Health Organization in 1988 and 2004, the number of people who lack access to essential medicines was virtually unchanged during the 16-year span. New medical technologies are irrelevant for poor people if they aren't accessible or affordable. Science innovation is pointless if marginalized people don't have access to already existing technologies or treatments.

In the current social and political context, a major investment in nanomedicine R&D may not be the right prescription for addressing human health needs, especially in the global South. History shows that new technologies do not solve complex problems rooted in

poverty and social inequities. Since the beginning of the 21st century, life expectancy has *decreased* in 38 countries worldwide. Even in North America and Europe where mortality rates steadily declined throughout the 20th century, studies have shown that those declines were largely independent of medical interventions and should be more correctly attributed to improved nutrition and hygiene.

Nano-enabled medicines and the zeal for performance enhancement technologies threaten to re-direct scarce medical R&D funds away from essential health needs. But there are even greater opportunity costs. The emphasis on medical solutions diverts attention and resources away from non-medical aspects of community health and wellbeing. Basic interventions that lead to improved sanitation and housing, access to clean water and education – for example – may ultimately lead to greater improvements in human health than cutting-edge medical technologies.

New medical technologies are irrelevant for poor people if they aren't accessible or affordable. Science innovation is pointless if marginalized people don't have access to already existing technologies or treatments.

Basic interventions that lead to improved sanitation and housing, access to clean water and education – for example – may ultimately lead to greater improvements in human health than cutting-edge medical technologies.

Box 1: *Health* Matters[1]

What is the definition of *health*? Is *health* synonymous with *wellbeing*? If not, how are they different? There are at least two approaches to thinking about health: health can be understood to refer to a normative functioning of the entire body and, implicitly, the absence of any illness or disease that results in sub-normative functioning – i.e., "medical health." Those who understand health in this way do not reject the idea that "social" conditions – such as a stressful job or living in a war-zone – can take a toll on health, but the focus, as well as the point of intervention, is always the body (e.g., how to treat the hypertension caused by a high-stress job or the clinical depression experienced by victims of war). According to the medical model, every sub-normative functioning body belongs to a "patient" for whom medical treatment is necessary to regain (or attempt to attain) normative functioning.

A second, broader approach to understanding health can be called the "social" model, where social and mental wellbeing are necessary for health – in addition to physical wellbeing / the absence of physical illness. According to the social model, a person doesn't have to be a patient with a body functioning sub-normatively to suffer from ill health. A woman who is a victim of sex discrimination on the job may have a body free of physical illness, but she would not be healthy, according to the social model. Since its beginnings in 1948, the World Health Organization has considered social and mental wellbeing necessary components of health.[2]

The implications of adopting one model of health over the other are enormous, and most obviously at the points of intervention. For example, using the social model, the possible interventions to help a

New nano-scale technologies are now offering more interventions to make our bodies physically stronger, smarter, longer-lasting.

How many of us are ready for Homo sapiens 2.0?

victim of social injustice (e.g., sex discrimination) attain health could include civil litigation, legislation and protest, among many others – whatever action would bring about social and mental wellbeing, optimally by changing the social structures that allowed the injustice to exist. It's possible to address an absence of social wellbeing from within the medical model, of course – either by treating the effects on the body (hypertension, depression, anxiety are a few possibilities) or by attempting to "cure" the patient of the condition relating to social ill health. In the medical model, the possible "cures" for a paraplegic who is a victim of discrimination and social injustice would be some kind of medical intervention – bionic legs instead of accessible buildings, for example.

New nano-scale technologies are now offering more interventions to make our bodies physically stronger, smarter, longer-lasting. Transhumanists, who embrace the notion that even the healthiest body can be improved through technology (see p. 15), have devised a new way to think about health. For them, every human body performs sub-normatively – unless that body has been "improved" with technological enhancements. Social wellbeing may be important to transhumanists, too, but it is achieved by intervening in the body's functioning. One obvious difficulty with the transhumanist approach is that the optimum state of health constantly changes depending on what the "enhancement industry" makes available to the market. We already know the dizzying pace of the computer software treadmill and how thoroughly we're shut out of cyberspace until we buy the latest upgrade. How many of us are ready for *Homo sapiens 2.0?*

1 This discussion is based on the work of Dr. Gregor Wolbring, University of Calgary. See, G. Wolbring, The Triangle of Enhancement Medicine, Disabled People, and the Concept of Health: A New Challenge for HTA, Health Research, and Health Policy, Alberta Heritage Foundation for Medical Research, HTA Inititiative # 23, December 2005, available on the Internet: http://www.ahfmr.ab.ca/publications/. Dr. Wolbring is a founding member of the Center for Nanotechnology in Society at Arizona State University (US), the Executive Director of the International Center for Bioethics, Culture and Disability (www.bioethicsanddisability.org) and a member of the Board of ETC Group.

2 http://www.who.int/about/en/index.html

Introduction

Nanotechnology refers to the manipulation of matter at the scale of atoms and molecules – where size is measured in billionths of meters. A nanometer equals one billionth of a meter. At the nano-scale (1-100 nm), materials can exhibit very different properties from materials of the same composition at a larger scale. Properties such as strength, conductivity, colour and toxicity can all change at the nano-scale – and properties can change within the nano-scale as well. By exploiting these nano-scale property changes, researchers seek to create novel materials with increased functionality.

Nanotechnology has been described as "the transformational technology of the 21st century."[4] Experts predict that nanotech will revolutionize manufacturing across all industry sectors and eventually "impact the production of virtually every human-made object."[5]

Medicine is just one sector that will be profoundly influenced by nano-scale materials and devices. This report examines medical applications of nanotech-enabled drugs, devices and diagnostic tools and assesses what role nanomedicine will play in addressing the health-related needs of marginalized communities, especially in the global South.

The Market and the Players

Worldwide, nanotech R&D in all sectors was approximately $9.6 billion in 2005.[8] Though frequently cited by companies, politicians and the media as the most promising area of nanotech research, nanomedicine has actually received less funding than other sectors such as nano-electronics and nanomaterials.

According to Lux Research Inc., about 17% of all nanotech funding in 2005, approximately $1.6 billion, was devoted to the "life sciences sector." (Although "life sciences" is broadly defined, Lux Research reports that the majority of investment in this category relates to nano-enabled medical uses.)[9]

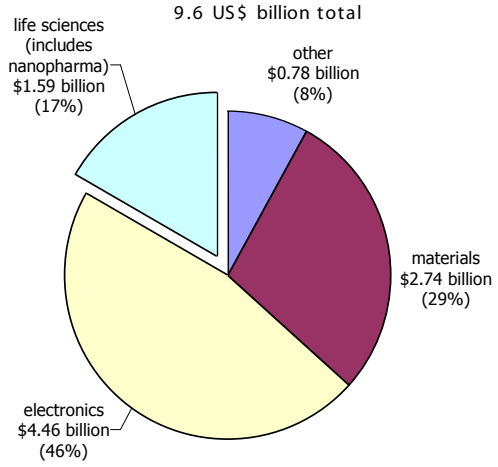
In the early days of nanotech (2001) the US government's National Science Foundation (NSF) predicted that nanotechnology "will help prolong life, improve its quality, and extend human physical capabilities," and that by 2010 or 2015 half of all pharmaceutical production – over $180 billion per annum – would be dependent on nanotech. More recently, Lux Research projected that the market for nano-enabled drug delivery systems will grow from $980 million in 2005 to about $8.6 billion by 2010. Nanotherapeutics (such as nanosilver for wound dressings) were $28 million in 2005 and will reach $310 million by 2010. The market for nano-enabled diagnostics will climb from $56 billion in 2005 to just over $1 billion by 2010.

What is nanomedicine?

The European Science Foundation defines nanomedicine as "the science and technology of diagnosing, treating, and preventing disease and traumatic injury, of relieving pain, and of preserving and improving human health, using molecular tools and molecular knowledge of the human body."[6]

The Canadian Institutes of Health Research broadly define nanomedicine as the specialized biomedical measurement or intervention – at a molecular scale – needed to treat disease or restore function.[7]

Worldwide Nanotech Funding by Sector 2005



Source: Lux Research. Inc

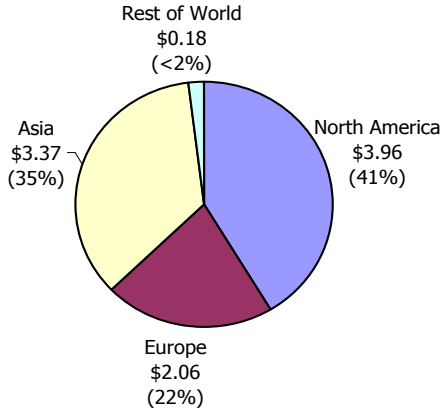
As of mid-2006, 130 nanotech-based drugs and delivery systems and 125 devices or diagnostic tests have entered preclinical, clinical or commercial development.

Big pharma is collaborating with nanobio start-ups, but since nanotech is still an unproven technology and the FDA approval process is uncertain, the major drug companies haven't made big investments yet.[14]

Nanotech is a nascent industry, but nano-enabled drugs and medical devices are already on the market, and there's a lot more moving down the tiny tech pipeline: According to *Nanobiotech News*, the nanomedicine and nanodevice pipeline shot up 68% from 2005 to 2006. As of mid-2006, 130 nanotech-based drugs and delivery systems and 125 devices or diagnostic tests have entered preclinical, clinical or commercial development; 75% of these products are being developed in the United States.[10] Other leaders in the field of nanomedicine include Canada, Australia and Israel. (See Table 1.) Industry analysts refer to the US Food & Drug Administration's January 2005 approval of Abraxane, a nano-based drug to treat breast cancer, as a "watershed event" for commercial nanomedicine.[11]

According to Lynn Yoffee of *Nanobiotech News*, "a third (30%) of all products are being developed as part of collaborations or licensing deals with a mix of pharma and biotech companies as their partners. But small nanobiotech start-ups and academic institutions remain the primary initial drivers of nanotech product development."[12]

Worldwide Nanotech Funding by Region, 2005
US$9.6 billion total



Source: Lux Research, Inc.

Governments, not corporations, are so far taking the lead in nanomedicine R&D. Of the estimated $1.6 billion devoted to nanotech R&D related to life sciences in 2005, a paltry 8% came from industry.[13] While the majority of Fortune 500 companies are investing in nanotech R&D, in the life sciences sector, the major pharmaceutical companies have taken a wait-and-see attitude – an approach reminiscent of the early days of biotech. Big pharma is collaborating with nanobio start-ups, but since nanotech is still an unproven technology and the FDA approval process is uncertain, the major drug companies haven't made big investments yet.[14]

One venture capitalist told *NanoBiotech News*, "One of the lessons learned during 2005 is to be careful about being 'nano' when going to the FDA. If you have a gold nanoshell, it should behave like a gold colloid. If it's a lipid, it should behave like an emulsion. From a regulatory perspective, you want to propose a familiar technology. Otherwise, you'll have to run a lot of extra tests."[15] Perhaps with this strategy in mind, some companies have even dropped the "nano" moniker: Nanopharma Corporation became Mersana Therapeutics, and Nanocure changed its name to Avidimer Therapeutics.

Between 2002–2007 the US government invested roughly $773 million in health-related nanotech R&D.[16] In late 2005, the US National Institutes of Health's National Cancer Institute (NCI) granted $26.3 million in first-year awards to establish eight Centers of Cancer Nanotechnology Excellence (CCNEs) as part of a five-year, $144.3 million project (2004-2009), known as the Alliance for Nanotechnology in Cancer.[17] The NCI's Alliance aims to "harness the power of nanotechnology to radically change the way we diagnose, treat and prevent cancer."[18]

From 2003-2008 the European Union's Sixth Research Framework Programme will devote 233.5 million Euros to nanomedicine-related projects.[19]

The Canadian government invested approximately CN$32 million in nanomedicine from 2000-2006 through its Canadian Institutes of Health Research (CIHR), which launched a Regenerative Medicine and Nanomedicine Initiative in 2003.[20] In 2006-07, CIHR expects to spend approximately CN$15 million on nanomedicine R&D.

The US Food & Drug Administration's January 2005 approval of Abraxane, a nano-based drug to treat breast cancer, was a "watershed event" for commercial nanomedicine.

Table 1: FDA-Approved Nano Drugs/Medical Products

Product/Manufacturer	FDA approval?	Purpose
Abraxane American BioScience, Inc.	January 2005	Nanoparticles containing paclitaxel used to boost the amount of anticancer drug available to kill breast cancer cells
Doxil Ortho Biotech Products (liposome-based delivery system developed by ALZA)	1999	Nanoparticle delivery system based on polymer-coated liposomes, dubbed "Stealth." Doxil is first product to incorporate this technology, for treatment of ovarian cancer.
Emend Merck – licensed technology from Elan	Approved	Nanoparticulate version of drug, aprepitant, to prevent nausea in cancer patients receiving chemotherapy.
Rapamune Wyeth – licensed technology from Elan	2000	Nanoparticulate formulation of sirolimus (Rapamune) to prevent organ rejection in patients receiving organ transplants
Silcryst Nucryst Pharmaceuticals/ product distributed by Smith & Nephew as Acticoat	Commercially available since 1998; FDA approved for over-the-counter use in 2001	Nanocrystalline silver incorporated in wound dressings because of its anti-microbial properties
SilvaGard AcryMed, Inc	December 2005	Catheter device coated with antimicrobial silver nanoparticles for internal use in body.
TriCor Abbott Laboratories– licensed technology from Elan	FDA approval Nov. 2004	Nanoparticulate formulation of TriCor – a drug to treat high cholesterol.
Verigene Nanosphere, Inc.	Awaiting FDA approval (as of 6/06)	*In vitro* product platform for testing sample of blood or saliva for the detection of nucleic acids and proteins at extraordinarily low concentrations.

"Nanotechnology will radically change the study of basic biological mechanisms and significantly improve the prevention, detection, diagnosis and treatment of diseases. One key to this potential is that nanotechnology operates at the same scale as biological processes, offering a unique vantage point from which to view and manipulate fundamental biological pathways and processes."

– Jeffery Schloss, Co-Chair, National Institutes of Health Nanomedicine Roadmap Initiative[22]

Why Nano?

Nanotech enthusiasts have high hopes that the technology will deliver uniquely effective treatments for illness and disease. The reason is simple: Nanotech operates on the same scale as biology. A molecule of DNA is about 2.5 nm wide and hemoglobin (a protein in the blood responsible for oxygen-transport) is about 5 nm in diameter. Human cells are much larger – on the order of 10-20 microns in diameter (10,000-20,000 nm) – which means that nano-scale materials and devices can easily enter most cells, often without triggering any kind of immune response.[21] The hope is that nano-scale particles, materials and devices can be designed to interact with biological materials in more direct, efficient and even precise ways. And because of their small size, they will be able to gain access to areas of the body – such as the brain and individual cells – that have proved difficult to reach with current technologies. (See p. 12.)

For example, the US government's National Cancer Institute writes that nanotech promises "access to the interior of a living cell [which] affords the opportunity for unprecedented gains on both clinical and basic research frontiers."[23] Being able to insert nano-scale probes into individual cells will advance understanding of the complex ways that cells work and may allow very early detection of aberrant cells heading in the direction of disease.[24]

Exploiting Quantum Effects

In addition, some nano-scale materials intended for biomedical applications will exhibit unusual properties that may increase their functionality. Substances that are smaller than about 100 nm can behave differently from larger particles of the same substance. Nano-scale materials may differ from their micro or macro counterparts in strength, colour, elasticity and/or toxicity; they may be able to conduct electricity more efficiently or they may be more chemically reactive. Optical, electrical or structural properties that are unique to the nano-scale are called "quantum effects." What's more, a substance's quantum properties can change *within* the nano-scale. Some nanoparticles of gold are inert, for example, while other gold nanoparticles of a different size are reactive. Shape matters, too. It is possible that a 20 nm spherical nanoparticle of a particular substance will be non-toxic to cells while a 60 nm rod-shaped particle of the same substance will produce a cytotoxic (toxic to cells) effect. There are no current models that can predict quantum effects, so a project is underway to try to characterize specific nanomaterials – to understand their physical attributes, their *in vitro* biological properties and their *in vivo* compatibility (using animals first).[25] The task of mapping out the entire new world of nano-scale materials is daunting, if not impossible, taking into account all the possible variations of substance, size, shape and surface structure.

Increasing Bioavailability

Not all medical applications of nanotechnology will exploit quantum effects, however. A drug in the form of a 400 nm particle may be more efficacious than its 2-micron counterpart because it may be more **bioavailable*** – i.e., useable by the body – or it may be able to gain direct access to a tumor, for example, but it most likely won't exhibit unique nano-scale properties. In general, only substances smaller than about 100 nm in at least one dimension exhibit quantum effects, though there are particular cases – such as **polymers** that have been reinforced with nanoparticles such that bonds form between the two materials – where special properties are exhibited at sizes larger than 100 nm.[26]

The ultimate vision is to combine nano-formulated drugs and **targeted drug delivery** with **personalized medicine** – an approach to health-management that relies on a patient's genetic profile to reveal individual predispositions to particular diseases or levels of receptivity to particular pharmaceutical agents. According to this vision, tomorrow's nanotech-enabled treatments could be multifunctional devices capable of detecting and identifying particular diseases on the cellular level and, at the right time, dispensing the correct drug in the correct dosage, tailored to the individual patient and reporting real-time information to monitor the status of the disease.[27]

Small-Scale Pharma

Nanotech has already changed the way some drugs are formulated, and in certain cases, reformulated. When a pharmaceutical compound is formulated as a nanoparticle, its level of bioavailability increases. In other words, the body can absorb a drug compound more quickly and easily – and therefore utilize it more effectively – when the compound exists on a scale closer to the scale of biological processes. A drug's level of bioavailability is a major factor in determining its efficacy. One market research firm estimates that $65 billion in annual drug revenues (almost 16% of total drug industry sales) come from pharmaceuticals with poor bioavailability, corresponding to higher patient costs, inefficient treatments and increased risk of toxicity.[28]

Elan Corporation, based in Dublin, Ireland, has developed a proprietary process for "milling" pharmaceutical compounds to produce small particles (typically less than 1000 nm) with increased bioavailability and faster rates of absorption, according to the company.[29] Elan also claims that the newly formulated nano-drugs eliminate "fed/fasted variability" (i.e., it matters less whether or not the drug is taken along with food). Big pharma companies such as Wyeth, Merck and Abbott have taken their proprietary compounds to Elan for milling. In most cases, the drugs have already been approved (by the US FDA) in larger form, and, as long as the companies can show "bioequivalence"[30] – that the difference in the action of the drug between the old and new formulations is "medically insignificant" – the new nano-version isn't subject to more regulatory scrutiny, such as additional clinical trials.

One market research firm estimates that $65 billion in annual drug revenues (almost 16% of total drug industry sales) come from pharmaceuticals with poor bioavailability, corresponding to higher patient costs, inefficient treatments and increased risk of toxicity.

* Words in **boldface** type within the text are defined in the Glossary on pages 47-48.

Pharma companies are already taking advantage of extended patent protection made possible by nanoparticulate formulations.

Pharmaceutical companies are relying on nanoparticulate formulations to boost the therapeutic value of "under-performing drugs," but they're also seeking to boost profits. It is possible that older drugs, no longer on the market due to low efficacy or potentially adverse side-effects in certain patient populations, could be made more effective or safer by reformulating at the nano-scale, significantly reducing the cost of the drug development process.

Pharma companies are already taking advantage of extended patent protection made possible by nanoparticulate formulations.[32] Even in the cases where bioequivalence between a drug and its nano-scale counterpart cannot be demonstrated, and additional clinical trials are necessary, there is a strategic advantage in the United States: The patent-holder is given three or five years of "non-patent exclusivity" while the drug undergoes new clinical trials.[33] This period is independent of patent rights and benefits big pharma because it keeps companies that produce cheaper, generic drugs at bay.[34]

"Nanotechnology is increasingly being used by a few forward-looking companies to breathe new life into old drugs by making them more effective…If pharmaceutical companies reformulated an existing drug instead of developing a new one, it [would substantially reduce development cost] while extending its patent-protected life cycle and yielding millions more in sales."

– Lux Research, Inc.[35]

Box 2: Is More Medicine the Right Weapon to Combat Disease?

In a landmark – though not one-of-a-kind – article from 1977, J.B. and S.M. McKinlay questioned the contribution of medical interventions to the decline in mortality rates seen in the US since 1900.[1] They concluded that, at most, 3.5% of the decline (1900-1973) could be attributed to medical interventions and presented data showing that in the case of many infectious diseases (e.g., tuberculosis, typhoid, measles and scarlet fever), medical interventions were introduced several decades after a marked decline in mortality had already set in. Other studies demonstrating a minimal impact of medical interventions on declines in mortality (focusing on Europe) preceded the McKinlays' and more studies followed. Though the assertion that medical interventions have had minimal impact on declining mortality rates was considered a "modern heresy" in 1977, the data – from studies both before and after the McKinlays' – proved the point so convincingly that by 2003 the minimal-impact thesis was considered "conventional wisdom."[2] This doesn't mean that it was enthusiastically embraced or even heard outside a small circle, only that it stood on firm statistical grounds. In general, the studies suggested that declines in mortality should be attributed more correctly to improved nutrition and reduced exposure through better hygiene.

Almost three decades ago, the McKinlays understood the profound implications of accepting or rejecting the thesis that medicine's contribution to declining mortality rates has been minimal:

> If one subscribes to the view that we are slowly but surely eliminating one disease after another because of medical interventions, then there may be little commitment to social change and even resistance to some reordering of priorities in medical expenditures… if it can be shown convincingly, and on commonly accepted grounds, that

> the major part of the decline in mortality is unrelated to medical care activities, then some commitment to social change and a reordering of priorities may ensue.[3]

It's not surprising that the measure of medicine's impact has become a contentious issue. Challenges to the minimal-impact thesis have recently begun to surface from within industry-connected academia.

In late 2003, Dr. Frank Lichtenberg, an economist at Columbia Business School (NY, USA), delivered a lecture at the Manhattan Institute's Center for Medical Progress. The Institute "turns intellect into influence" and the Center's mission is "to articulate the importance of medical progress and the connection between free market institutions and making medical progress both possible and widely available throughout the world."[4] Lichtenberg reported on a study in which he compared the launches of new drugs and disease-level data across 52 countries from 1982-2001 and found that "new drugs increase the longevity of the average person [suffering from the disease targeted by the new drug] by about three weeks per year."[5] His findings led him to conclude that the increased longevity he attributed to new drugs was well worth society's investment. More recently (March 2006), Lichtenberg amassed data on the effect of the introduction of new laboratory procedures and other medical innovations in the US between1990-2003. He concluded that "conditions with higher rates of lab and outpatient drug innovation had larger increases in mean age at death," supporting his hypothesis that "the more medical innovation there is related to a medical condition, the greater the improvement in the average health of people with that condition."[6] (This assumes, of course, that the average person has access to the innovation.)

Are we to conclude from the earlier studies and Lichtenberg's recent work that medical interventions began to have an impact on improvements in health only in the last two decades of the twentieth century? If yes, how do we explain the sudden change? Much more than an academic exercise, accurately determining the return on investment in new medical interventions should have a major impact on public policy by helping to establish spending priorities, including R&D priorities. The US National Institutes of Health, for example, must decide how best to divvy up more than 28 billion taxpayer dollars annually. But how do policymakers ensure they have access to data and analysis that is as disinterested as possible? Lichtenberg, for example, lists pharma giants Pfizer and Merck among his funding sources and has consulted for the National Pharmaceutical Council.[7] Could he unwittingly be serving the interests of the medical industry? Policymakers, and society in general, must find ways to gain a full understanding of the historical impacts of medical technologies – and the potential impacts of technologies now under development. (See ICENT on p. 45, below.)

"… if it can be shown convincingly, and on commonly accepted grounds, that the major part of the decline in mortality is unrelated to medical care activities, then some commitment to social change and a reordering of priorities may ensue."

The Downside to Nano's Novelty and Mobility

Ironically, the qualities that make nanomaterials so attractive to researchers and industry across a wide range of fields, including medicine – their small size, mobility and unusual properties – may turn out to be the same qualities that make them harmful to human health.

The extra-ordinary properties of nano-scale materials have raised hopes for vastly more effective medical treatments and improved diagnostics, including more precise imaging. Because of their small size, nanomaterials could gain easy access to individual cells and to areas of the body out of reach of current therapies. The quantum effects – unusual optical, electrical or structural properties unique to the nano-scale – exhibited by some nano-materials may increase the materials' functionality. (See quantum dots, below.) Ironically, the qualities that make nanomaterials so attractive to researchers and industry across a wide range of fields, including medicine – their small size, mobility and unusual properties – may turn out to be the same qualities that make them harmful to human health.

There is a virtual consensus among scientists that the toxicology of engineered nanomaterials is largely unknown, and that toxicity data cannot be extrapolated from existing toxicology studies conducted on larger scale particles.[36] In other words, the toxicity of a substance in the form of a particle one-micron in diameter will very likely differ from the toxicity of a particle (of the same substance) that is only 10 nm in diameter (1 micron = 1000 nm). This is because the smaller the particle, the greater percentage of its atoms are on the surface. A large surface area corresponds to a high level of reactivity – and, in general, the more reactive a substance, the more toxic it is. What is generally true, however, may not necessarily hold true within the nano-scale. The behavior of materials in this size range (~1-100 nm) is unpredictable and scientists have recently suggested that a nanomaterial's shape and surface structure are also important factors in reactivity and toxicity, making the field of nano-toxicology even more challenging.[37]

The knowledge gap requires urgent attention because there are hundreds of products that contain nanomaterials already on the market,[38] and no federal agency in the world regulates nano-scale materials *per se*.

The increased bioavailability associated with nano-scale materials means that dosages of nano-formulated drugs will need to be very carefully monitored, since they "pack more of a punch" than their larger scale counterparts – overdosing could lead to serious problems. Likewise, increased mobility could also be a drawback. Access to the brain is especially useful when treating brain cancers, for example; on the other hand, not all engineered nanoparticles to which we will be exposed – via the environment or commercial nano-products – should be allowed free rein in our bodies. A recent study suggests that the increased reactivity of titanium dioxide (TiO_2) nanoparticles, which are frequently used as an ingredient in sunscreens, can cause damage to brain microglia – cells whose purpose is to protect the central

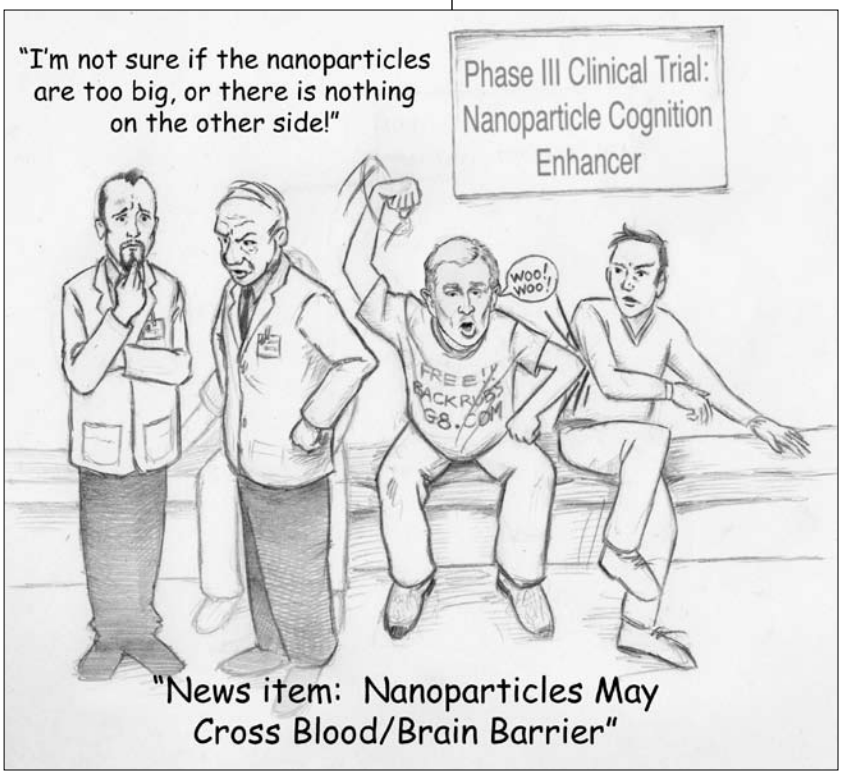
nervous system.[39] Despite the fact that many commercial sunscreens and cosmetics contain engineered nanoparticles, including TiO_2, there is no scientific consensus on the degree to which nanoparticles can penetrate the skin. Even those nanomaterials intended to enter our bodies as targeted drugs or imaging agents could create problems if they stray from their targets and take up permanent residence in our cells, brains or other organs.

Assessing nanotech's prospects in the health sector, Frost & Sullivan, an international market research firm, cautions, "[N]ano-particles and nano-materials used for drug discovery applications can become a cause for concern if they degrade too rapidly or if they remain in the body for prolonged periods. The ability of nano-materials to interact with biological organisms leads to the possibility that they may be harmful to humans and the environment…Current understanding of the potential toxicity of nanoparticles is limited, but research indicates that some of these products may enter the human body and become toxic at the cellular level, in various body fluids, tissues and/or organs."[40]

Particles Without Borders?

Can inhaled nanoparticles reach the central nervous system? Can nanoparticles in cosmetics and sunscreens penetrate through layers of skin? Cross the blood brain barrier? How small must they be to enter cells? To what extent nanoparticles translocate (move from one place to another) in the body is not at all clear. It seems that a particle's size, composition and shape all play a role. One recent study, for example, showed that spherical particles – some with a diameter of 14 nm and others 74 nm in diameter – entered cells more easily than rod-shaped nanoparticles measuring 14 nm x 74 nm.[41] Spherical 50 nm particles, however, were twice as likely to enter cells than spherical particles that were slightly larger *or* slightly smaller.[42] A study on rats has shown that inhaled nanoparticles smaller than 40 nm can reach the brain (specifically, the olfactory bulb) via the olfactory nerve.[43] This finding is potentially significant for both drug delivery development and nanotoxicology because it suggests that nanoparticles may be able to circumvent the notoriously tight blood-brain barrier.

The knowledge gap requires urgent attention because there are hundreds of products that contain nano-materials already on the market, and no federal agency in the world regulates nano-scale materials per se.



It is in the realm of human performance enhancement technologies (dubbed "HyPEs") that convergence will perhaps make its greatest impact and greatest profit.

"Nanotechnology can go beyond the limitations of biology."

– Ray Kurzweil in *Scientific American*, July 2006

From Therapy to Enhancement: HyPEd-Up *Homo sapiens*

Will nano-scale technologies be used to combat health?

While governments, industry and scientists – particularly in OECD countries – are quick to point out the potential contributions of nanotech to improve ill-health, advances in "converging technologies" – including the fields of nanotech, biotech, information technology, neurotechnology and the cognitive sciences – are poised to address less-than-optimum health or *perceived* ill-health. It is in the realm of human performance enhancement technologies (dubbed "HyPEs") that convergence will perhaps make its greatest impact and greatest profit.

Technological convergence will make it theoretically possible to augment the structure, function and capabilities of human bodies and brains. The vision is not simply of disability eliminated and illness cured, but of stronger, faster bodies that out-perform the healthiest and most athletic bodies of today, with brains re-vamped to retain more information and to communicate directly with computers, artificial limbs or with other brains. An example is an artificial neuron implant, already approved by the FDA for clinical use, which replaces neurons that have been damaged by Parkinson's disease. The device allows software upgrades to be downloaded directly from an *ex vivo* computer to the implant in the body.[44] For now, these devices are reserved for those suffering from disease; in the near future, it will be harder to tell what is a disease and what is merely less-than-optimum health, to distinguish between therapy and enhancement. (See BANG, pp. 22.)

For a grand finale, the new and improved body created through converging technologies could extend the human life span to well over a century. According to the US government, technologies converging at the nano-scale will "improve human performance" in the workplace, on the playing field, in the classroom and on the battlefield. Uploadable intelligence, downloadable memories and hyper-performing bodies may require a revised definition of our species, *Homo sapiens*. Or perhaps the new technological realities will create a need for a new species classification altogether (*Homo sapiens 2.0*), describing the small fraction of the global population that will be able to pay to be enhanced through converging technologies.

While relatively few will be able to afford the full enhancement package, some enhancements enabled by converging technologies will become more and more pervasive and "naturalized" until they are viewed as necessary corrections in the way that eyeglasses are today. At the same time, there will be a corporate push to define and broaden the scope of treatable "health conditions" – often under the guise of "raising public awareness" – in order to create or expand markets for newly-available enhancements.

The practice of promoting illness in order to create markets for treatment is called **disease-mongering**.[45] Certain personality traits (e.g., shyness), physical traits (e.g., "average" strength or height), cognitive traits (e.g., "normal" intelligence) will be deemed undesirable and correctable (and gradually unacceptable, not to be tolerated). The line between enhancement and therapy – already blurry – will be completely obliterated. The ultimate effect will be a shift in the perception of what is "normal" and the creation of what Dr. Gregor Wolbring, a biochemist and health researcher at the University of Calgary, calls an "ability-divide."[46] Like the digital divide, the ability divide will shadow the boundary between North and South, and between rich and poor everywhere. Under the present policy conditions, the introduction of pervasive human performance enhancement technologies – HyPEs – is likely to result in a new group of marginalized people and an accompanying "divide."

Some maintain that it is possible to draw a line between therapy and enhancement and that a line *should* be drawn because the distinction will help inform an ethical debate about what it means to be human and how to best preserve our human-ness.[48] Others have argued that, given society's current configuration, a line between therapy and enhancement cannot be maintained and an inclusive debate should begin by recognizing the social factors (e.g., values, prejudices) that currently contribute to our understanding of what it means to be human. From there, the debate should focus on how or if to protect those who do not currently meet the "human" standard – and those who will not meet a revised standard in our technologically-enhanced future.[49] Still others – **transhumanists**, for example, who believe the human species is in a comparatively early phase of development – are comfortable with a malleable definition of *Homo sapiens* and are eager to make use of available technologies that may bring about "better" humans.[50] (See p. 22.) They envision a world not far off where a "cure" for the "medical condition" known as "aging" – perhaps through the advancement of "SENS," Strategies for Engineered Negligible Senescence (Aging) – is found and humans live in good health far longer than 100 years.[51] While some transhumanists acknowledge that the introduction of ubiquitous enhancement technologies could widen the gap between rich and poor, they do not see that as a compelling reason to limit their use. They view disparities within society as a separate and long-standing problem not created by (nor solved by) enhancement technologies.[52]

A Workout on the Enhancement Treadmill: Can we get off?

Most enhancements are welcomed into society as much-needed cures or treatments benefiting a population identified as ill or disabled. A few are developed for particular "well" populations with specialized needs, such as soldiers in combat. Though enhancements are ostensibly intended for limited consumption, the usual pattern

"Every technology has led to a new group of marginalised people and to new inequalities. There is no reason under today's policy realities why this would be different if the human body becomes the newest frontier of commodification. As much as human enhancement technology will become an enabling technology for the few, it will become a disabling technology for the many… If we go on as we are today we will see the appearance of a new underclass of people – the unenhanced."[47]

– Dr. Gregor Wolbring, University of Calgary

Like the digital divide, the ability divide will shadow the boundary between North and South, and between rich and poor everywhere.

is that use increases dramatically soon after introduction, beyond the population that first justified the enhancements' development. When that happens, there are real-world consequences that society has not fully anticipated.

Genetically engineered human growth hormone, for example, won FDA approval in 1985 to treat dwarfism – a condition characterized by abnormally short stature and most often caused by a spontaneous genetic mutation.[53] Today human growth hormone is prescribed to (and FDA approved for) healthy children whose parents judge them to be too short. Their children, they say, suffer from "Idiopathic Short Stature," meaning they exhibit no signs of illness; they're simply unacceptably short. Growth hormone is now widely used by athletes of all sizes seeking performance enhancement. Growth hormone is also heavily promoted as having anti-aging properties.[54] The "treatment" is not cheap – growth hormone can cost $20,000 a year and is usually prescribed for four or five years.[55] The global market is estimated to be about $2 billion annually.[56]

Expanding the use of growth hormone to healthy populations is problematic. As Dr. Michael Freemark explains in an editorial in *The Journal of Clinical Endocrinology & Metabolism*, "The term 'idiopathic short stature' carries the implication of disease [though] the major liability of short stature is susceptibility to discrimination. But discrimination is a 'disease' of society, not of the short individual. In theory, societal intolerance should be addressed by enacting and enforcing antidiscrimination laws, reeducating the public, and counseling the family rather than by medicating the child."[57]

Freemark goes on to demonstrate how the introduction of an enhancement can shift society's perception of what is abnormal and/or acceptable. He writes, "In the absence of disease, there is no rationale for defining a cutoff for treatment. For example, how does one justify treating a boy whose height prediction is 5 ft. 3 in. but not one whose height prediction is 5 ft. 3 and 1/32 in.? More important, the use of GH [growth hormone] in very short children may create an unending cycle of catch-up; increases in the ultimate heights of very short children would necessitate reclassification of some previously normal children (short but with height predictions exceeding current cutoffs) as 'idiopathically short.' **This may be the only circumstance in which treatment of one group of children creates illness in another previously healthy group."** (emphasis added)

Unfortunately, growth hormone won't be the only case in which a HyPE technology administered in the absence of disease will create a "diseased" population that had previously been considered healthy. Consider the following examples:

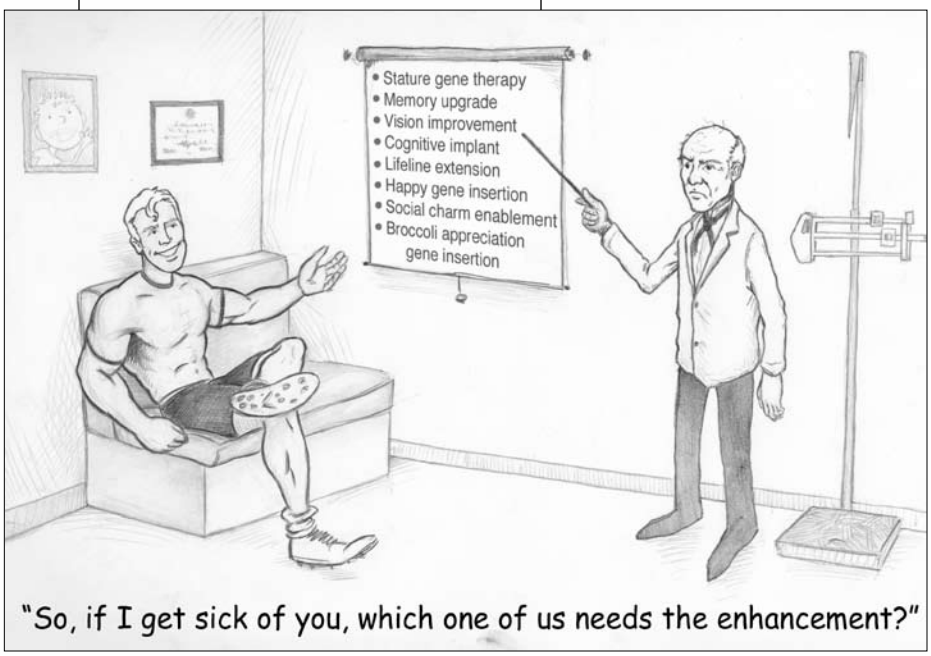
- **Transcranial Magnetic Stimulation (TMS):** TMS is a procedure that stimulates areas of the brain externally using an electromagnetic field. TMS can help reveal the functions of activated (or de-activated) parts of the brain, but is also considered a potential treatment for disorders of the brain,

including Parkinson's and even depression. Using magnetic fields to stimulate (or turn off) different parts of the brain, researchers have discovered that "normal" people can dramatically increase their brain power. A recent study conducted by Professor Allan Snyder at the Centre for the Mind – a joint venture of the Australian National University and the University of Sydney – showed that repetitive TMS of the left anterior temporal lobe improved the ability of participants to guess the number of elements shown on a computer screen. The skill receded an hour after the stimulation.[58] Will it be long before workers are taking TMS breaks instead of coffee breaks? Will brain stimulation be seen as necessary to maintain a competitive edge in the workplace? How big a brain boost will be big enough?

- **Sleep deprivation treatments:** These aren't meant to help sufferers of insomnia and other sleep disorders; in fact, they are meant to make sleep deprivation sustainable. The US military is on the front line of sleep deprivation research and has funded dozens of projects, including studies on the potential use of TMS to reduce the need for sleep.[59] DARPA (US's Defense Advanced Research Projects Agency) explains its particular interest in making sleep deprivation possible: The success of military operations "depend[s] upon the warfighter's ability to function for extended periods of time without adequate sleep."[60] Along with TMS, will sleep deprivation become a way of life for those who seek competitive advantage and can afford the treatments / drugs? Will workers – such as truck drivers, for example – be required to undergo sleep deprivation "therapy" so they can stay on the clock longer hours? What will be the societal (and health) effects of an army of "the living dead" or a growing population of the perpetually sleep deprived?

- **Laser eye surgery:** In some cases, it is now possible to restore faulty vision to a perfect 20-20 through corrective eye surgeries. Millions of surgeries are performed every year (an estimated 1.6 million in 2005 in the US alone).[61] The number of surgeries is rising, and the increase is expected to continue. Given that most people don't consider eyeglasses to be an elective "enhancement," are there potential societal impacts of widespread perfect vision – or better-than-perfect vision – that need to be considered? *The New*

Unfortunately, growth hormone won't be the only case in which a HyPE technology administered in the absence of disease will create a "diseased" population that had previously been considered healthy.



York Times recently noted that the Naval Academy in the US has offered corrective eye surgery to all midshipmen (whose sight can benefit from it) free of charge for the last five years.[62] Fewer than 30 percent of the class of 2006 refused the surgery (the number of refusals has dropped every year). An unintended consequence has been that, each year during the same five-year period, the Naval Academy has missed its annual quota for supplying the Navy with submarine officers. Submarines have traditionally been the second choice for promising personnel with less than perfect eyesight. Aviation – the first choice of naval officers, which requires perfect vision – is now a viable option for more people. As these and other more extreme enhancements become widespread in the general population, what societal shifts can we expect? How will we deal with those impacts we

Table 2: Selection of Technologies with HyPE Applications or HyPE Potential

This table presents a selection of technologies that are currently available or are under development. Those cases in which nanotechnology is explicitly used are noted in the table. Some technologies were/are being developed with enhancement in mind; in the case of others, the enhancement-potential was exploited/will be exploited after development. The list is not comprehensive and whole categories of enhancements have been omitted (e.g., cosmetic surgery, tissue engineering).

Product	Company	On the Market?	Initial usage	Other usage
Oral/Topical Medications, including Cognition Enhancers				
Beta-adrenergic blocking agents (beta-blockers)	Various companies	Yes	Congestive cardiac failure	Anxiety-reduction, e.g., taken by orchestra musicians pre-performance
Aurorix (active ingredient: moclobemide)[1]	F. Hoffman-La Roche	Yes	Antidepressant	Social phobias
Selective Serotonin Re-uptake Inhibitors (SSRIs), e.g., Celexa, Desryl, Effexor, Luvox, Paxil, Prozac, Serzone, Zoloft, etc.)	Various companies	Yes	Antidepressant	Anxiety disorders (e.g., Generalized Anxiety Disorder, Panic Disorder, Social Phobias (e.g., shyness), Obsessive-Compulsive Disorder, Post-Traumatic Stress Disorder
Rogaine (active ingredient: minoxidil)	Pfizer	Yes	Control high blood pressure[2]	Promote Hair growth
Viagra (active ingredient: sildenafil)	Pfizer	Yes	Treat erectile dysfunction, impotence	Sexual performance enhancement
HT-0712 (a phosphodiesterase-4 inhibitor)	Helicon Therapeutics, Inc. (US), Inflazyme Pharmaceuticals (Canada)	Phase IIa clinical trial	Treat Alzheimer's disease, Age Associated Memory Impairment	Expected to be used in various contexts that require mental alertness
Alertec (Canada), Provigil (US) (active ingredient: modafinil)	Cephalon	Yes	Treat Narcolepsy	Treating Apnea/ hypopnea syndrome (OSAHS), "shift work sleep disorder" (SWSD), depression, Multiple Sclerosis, Alzheimer's; allowing soldiers to go without sleep
Aricept (active ingredient: donepezil HCl)	Pfizer, Eisai Co., Ltd	Yes	Treat Alzheimer's	Experimentally, used by airplane pilots to improve recall of complex air traffic control commands[3]

Product	Company	On the Market?	Initial usage	Other usage
Various cognitive enhancers	Various Companies	>40 in clinical development[4]	Treat Mild Cognitive Impairments (MCIs), Alzheimer's, Age Associated Memory Impairment	Expected to be used in various contexts that require mental alertness
SPI-1005	Sound Pharmaceuticals (US)[5]	Phase I clinical trial	Prevent and treat noise-induced hearing loss	
"Invasive" Brain-Machine Interfaces				
Braingate Neural Interface System[6]	Cyberkinetics Neurotechnology Systems Inc. (USA)	Pilot clinical trial	Sensor implanted on the motor cortex coupled with device that measures and interprets signals from the brain; allows a person to control a computer with thought in order to initiate a range of activities	
"Non-Invasive" Brain-Machine Interface				
MAIA – Mental Augmentation through Determination of Intented Action[7]	IDIAP (Switzerland), Katholieke Uni Leuven (Belgium), Uni Hospital of Geneva, Fondazione Santa Lucia-Rome, Helsinki University of Technology	In development	Using thought (EEG brain signals) to control a wheelchair in an indoor environment; control a robot arm; handle emergency situations (e.g., braking a vehicle or retracting the robot arm)	
Virtual Helmet[8]	University College London	In development, 2011-2016	Brain waves (EEG signals) translated into actions, allowing severely disabled people to control wheelchairs, computers and artificial limbs through thought	
Mental Typewriter, Berlin Brain-Computer Interface (BBCI)[9]	Fraunhofer Institute and Charité Campus Benjamin Franklin (Berlin)	Prototype	EEG signals are amplified and transmitted to the computer in order to choose letters (through moving a computer's cursor) by thought.	
Galvanic vestibular stimulation[10]	Nippon Telegraph & Telephone Corp. (Japan)	In development / prototype	Affecting a person's sense of balance by applying low voltage electric current to the ears through a special headset; for entertainment or as aid to those with balance problems	Warfare: Defense contractor (Invocon, TX, US) is exploring whether electromagnetic pulses could be fired into people's ears to subdue them
Cortically coupled computer vision system, known as C3 Vision[11]	Columbia University, with funding from Defense Advanced Research Projects Agency (US)	In development / prototype	While EEG cap wearers watch streaming images or video footage, a computer tags images that elicit a brain signal and ranks them in order of the strength of the signal. Afterwards, only the information that was tagged is reviewed; intended for monitoring and intelligence gathering	

Product	Company	On the Market?	Initial usage	Other usage
Brain-Brain Interface				
Electrodes implanted in arms, linked by radio signals to a computer, connect nervous systems of Kevin and Irena Warwick[12]	University of Reading (UK)		Early stage of computer-linked "global brain"	
Bionic Body Parts				
Bionic Ear, including software upgrades[13]	Various companies, including Advanced Bionics, Cochlear, Inc. (Australia), MED-EL (UK), Laboratoires MXM (France)	Yes	Restore hearing to those with severe to profound hearing loss	In the future, bionic body parts may be used by those now called 'disabled' and those considered 'healthy' today to provide above-the-norm abilities
Bionic Leg	Various companies, including Otto Bock HealthCare (Germany), Victhom Human Bionics (Canada)	Yes	Replace legs of amputees or those born without legs and feet	
Bionic arm[14]	US DARPA's Revolutionizing Prosthetics Program	Clinical testing planned for 2009	Replace arms of amputees	
Bionic eye[15] (artificial retinas, retinal prostheses)	Various companies and universities, including Second Sight Medical Products (US), VisionCare Ophthalmic Technologies (US), IIP-Technologies GmbH (Germany), Sumipro (Netherlands); Univ. of Texas (US) attempting to replace light-sensing nerves with a combination of nanoparticles and carbon nanotubes[16]	In development; some in limited clinical testing, some on market by 2008;	Restore vision	
Bionic knee	E.g., "Rheo Knee" – Ossur (Iceland)[17]	Yes	Replace damaged knees	
Bionic hand, "Cyberhand"[18]	European university consortium	In development, available late 2007	Replace damaged/ missing hands	
Reconstructive brain surgery, using nano-scale fibers to connect gaps in brain caused by damage[19]	MIT (US), Hong Kong University, and Fourth Military Medical University in China	In development; human trials ~2009	Restore lost abilities to stroke victims and others	
Artificial bone from ceramic composites[20]	Materials Science Division at Lawrence Berkeley National Laboratory (US)	In development	Improve bone grafts for hip and knee replacements	
Neuroimplants (to the Central Nervous System)				
Artificial Hippocampus[21]	Various US universities	In development; ~2019	Silicon chip that mimics the part of the brain responsible for making memories; initially used to treat Alzheimer's	Could be used in the future to upload information into the brain

Product	Company	On the Market?	Initial usage	Other usage
Implanted Neurostimulators (Deep Brain Stimulators, see also Transcranial Magnetic Stimulation, below)[22]	St. Joseph's Hospital (US); New York University/ MIT collaboration using nanowires to connect stimulating device to brain (US);[23] Bristol University and the Queen Elizabeth II Hospital in Welwyn Garden City (UK), among others	Yes (nano-wire deep brain stimulators in develop-ment)	Pacemaker-like device implanted in chest plus flexible wires implanted in brain; electrical impulses sent from "pacemaker" to brain in order to treat Parkinson's, migraine headaches and chronic pain	Depression, obsessive-compulsive disorder, improve mobility of stroke victims, curb cravings in drug addicts
Vagus Nerve Stimulation (pacemaker-like generator implanted in chest sends electrical pulses through the vagus nerve in the neck to the brain)[24]	Cyberonics, Inc.	Yes	Epilepsy seizure control	Treatment-resistant depression (approved 2001 in Canada and Europe; 2005 in US
Anti-Nogo-A antibodies[25]	Novartis Pharma, among others	Clinically tested on 15 patients; trial of 100 patients planned 2007[26]	Injecting antibodies in spinal cord to neutralize Nogo-A (growth inhibitor) post-injury to encourage nerve re-growth	
Others				
Genetically modified *Streptococcus mutans* bacterium to prevent tooth decay[27]	University of Florida (US)	Clinical trials completed with denture-wearers; on market in ~3-5 years	One-time oral spray to prevent cavities and tooth decay	
Subvocal speech recognition[28]	NASA (US)	In develop-ment, prototype	Electrodes attached to throat recognize movements of muscles associated with word formation rather than sound; being developed for astronauts, underwater communication, emergency workers in loud environments	
RFID [radio frequency identification] chip implant[29]	Verichip (US) RFID implants are FDA approved	Yes	Surveillance, identification, tracking of humans (workers, children, etc.)	
Magnetic implants in fingertips[30]	Independent research by "body- modders" (modifiers)	Yes	Enhancement of touch sensations	
Eyeglass lenses improving 20/20 vision two-fold[31]	PixelOptics (US)	Prototype ~Feb. 2007	US Dept. of Defense granted $3.5 million to PixelOptics to develop for military uses	
Chip implanted at tooth root to emit low intensity pulsed ultrasound (LIPUS)[32]	University of Alberta (Canada)	Prototype, on market ~mid-2008	Stimulate root to promote tooth re-growth	
Hybrid assistive limb ("HAL")[33] – motor-driven "exoskeleton" strapped onto legs; backpack holds computer w/ wireless network connection, batteries on belt	University of Tsukuba / Cyberdyne, Inc. (Japan)	Prototype; on market in 2007?	Enable those with gait disorders to walk	Expected to be used by soldiers, disaster relief workers
Berkeley Lower Extremity Exoskeleton ("Bleex")[34]	Berkeley Robotics and Human Engineering Lab (US)	Prototype; in develop-ment	Enhance strength and endurance of emergency workers	Warfare: "Bleex" project funded by DARPA (US)

Sources: Dr. Gregor Wolbring, University of Calgary; ETC Group. See notes on page 55.

BANG Technologies:

Nano makes convergence possible. Will it lead to "better humans?"[63]

The current version of utopia brought about through technological convergence is being enthusiastically endorsed and heavily financed by governments and industry around the world.

haven't anticipated?

Some of us are already used to taking photographs, sending them to a friend and searching Google – all on our mobile telephones. But this all-in-one ethos extends beyond the realm of communication and information technologies. For a half-decade now, we've been hearing about high-level plans to overhaul the practice of science and technology through technological convergence, made possible by advances in nanotechnology. The ultimate goal is to intervene in all macro level phenomena – including environmental, biological and societal – by mastering control of nano-scale phenomena.

The quest for a "fundamental technology" giving humans control over nature is nothing new. Its roots go back at least to Francis Bacon's *New Atlantis* (published 1627),[64] in which he describes the fantasy island utopia of Bensalem where it is possible, for example, to "make by art…trees and flowers to come earlier or later than their seasons, and to come up and bear more speedily…and their fruit greater and sweeter, and of differing taste, smell, color and figure… and to make diverse plants rise by mixtures of earths without seeds…and to make one tree or plant turn into another."[65] The technological tweaks to Bensalem's flora and fauna are not random or unpredictable but are controlled ("Neither do we this by chance, but we know beforehand of what matter and commixture, what kind of those creatures will arise").[66] In language that will sound familiar to readers of US National Science Foundation (NSF) documents, the ultimate goal of the utopia is "the knowledge of causes… and the enlarging of the bounds of human empire, to the effecting of all things possible."[67] Compare, for example, the NSF's utopic vision of technological convergence almost four centuries later: "We envision the bond of humanity driven by an interconnected virtual brain of the Earth's communities searching for intellectual comprehension and conquest of nature."[68]

The current version of utopia brought about through technological convergence is being

Nanotechnology – controlling matter through manipulation of **Atoms** –

can converge with

Biotechnology – controlling life through manipulation of **G**enes –

can converge with

Information Technology – controlling data through manipulation of **B**its –

can converge with

Cognitive Neuroscience – controlling minds through manipulation of **N**eurons.

enthusiastically endorsed and heavily financed by governments and industry around the world. In the US, technological convergence is most often referred to as NBIC (an acronym derived from the technologies involved: nanotechnology, biotechnology, information technology and cognitive sciences).[69] In Europe, the vision of convergence is called CTEKS (converging technologies for the European knowledge society). In Canada, convergence is known as BioSystemics Synthesis.[70] Without necessarily sharing the enthusiasm and optimism of governments, civil society has come up with its own name for technological convergence, calling it BANG – from *Bits, Atoms, Neurons and Genes*, which are the operable units of the "NBIC" technologies.[71]

A theoretical instance of convergence might be the development and delivery of a drug to treat Alzheimer's disease: Suppose it is discovered, after sifting through mountains of data, that a natural compound existing in short supply in the Amazon may be effective in treating certain neurological disorders. Using recombinant DNA technology, researchers are able to produce the compound in large quantities. A nano-scale device enables the drug (discovered and produced using information technology and biotechnology) to be delivered to damaged neurons in the brain. While not every product of convergence will involve every one of the BANG technologies, most will use one or more technology that has been enabled or augmented by nanotechnology. Other examples of convergence might be implanted nanomaterials that replace bones damaged by arthritis, engineering neurons so they are able to control the movements of a computer's cursor or cognitive implants that can increase our brains' ability to store and use information.

A 2003 report of the Science & Technology Foresight Pilot Project (sponsored by Canada's National Research Council) identified five characteristics that make BANG technologies particularly consequential: *convergent* (meaning they can combine with one another but also that they can be applied across many different industrial sectors and research disciplines), *fundamental*, *replicant* ("each of these technologies has some capability to 'reproduce' itself"),[72] *distributed* (they can be used by individuals) and *public interest* (meaning that they all "will hold much promise, but at the same time be very disruptive").

As the lens through which the US government – and subsequently, European and Canadian governments – have viewed BANG is "improved human performance," debates about the ethical, social and economical implications of enhancement and life extension are crucial.

"Human life expectancy was only 37 years in 1800. Our ability to reprogram biology will dramatically increase it again, but this progression will be much faster. I expect that within 15 years, we will be adding more than a year annually to remaining life expectancy. So my advice is: take care of yourself the old-fashioned way for a while longer, and you may get to experience the remarkable century ahead in full."*

– Ray Kurzweil, "Reprogramming Biology," *Scientific American*, July 2006

*Kurzweil's current health management regime is no where near old-fashioned. He writes that he takes 250 supplements a day, gets therapeutic injections every week and routinely samples his blood, hair and saliva to monitor his body's levels of nutrients, hormones and metabolic by-products.[73]

"…current government policies and company strategies including incentive and funding mechanisms, both in developed and developing countries, have not generated sufficient biomedical innovation relevant to the needs of most developing countries. New, and even existing, treatments remain unavailable and unaffordable to those who need them."

WHO Commission on Intellectual Property, Innovation and Public Health, April 2006

What role will nano-enabled medicine play in addressing sickness and poverty in the global South?

"Some day soon, in a remote village in the developing world, a health worker will put a drop of a patient's blood on a piece of plastic about the size of a coin. Within minutes, a full diagnostic examination will be complete including the usual battery of blood work tests, plus analysis for infectious diseases such as malaria and HIV/AIDS, hormonal imbalances, even cancer. That remarkable piece of plastic is called a lab-on-a-chip and it is one of the revolutionary products and processes currently emerging from nanotechnology research with the potential to transform the lives of billions of the world's most vulnerable inhabitants." – News Release, University of Toronto, Joint Centre for Bioethics, 31 March 2005[74]

In September 2000, the United Nations adopted eight Millennium Development Goals (MDGs) and eighteen Targets – a roadmap for eradicating hunger and poverty and ensuring health and environmental sustainability, especially for the world's poorest, by 2015. The UN identifies three MDGs and eight (of 18) Targets as health-related. (See Box 3.) The UN Millennium Project's Task Force on Science, Technology and Innovation considers nanotechnology an important tool for achieving the MDGs.[75] Many others – scientific researchers, entrepreneurs, market analysts and rural development experts among them – agree that nano-scale technologies offer the potential to improve health globally – including in the developing world.[76] Advocates believe that nanotech could play an important role in addressing health in the global South – not just directly, by treating sick people with novel vaccines and nano-based therapies – but also indirectly, by alleviating conditions leading to disease, such as unsafe drinking water. Current research on nano-filters and nanoparticles that remove contaminants from water are oft-cited examples of nanotech's potential contributions to health in the developing world. ETC Group acknowledges that nanotech R&D related to water is potentially significant for the developing world. Access to clean water could make a greater contribution to global health than any single medical intervention. Nanowater research and its political and economic context require further study, and ETC Group will examine water-related nanotech R&D in a separate report. In this report, however, we confine our analysis to nanomedicine – drugs and devices to detect, diagnose and treat disease at the molecular level.

ETC Group believes that the global health crisis doesn't stem from a lack of science innovation or medical technologies; the root problem is poverty and inequality. New medical technologies are irrelevant for poor people if they

aren't accessible or affordable. Science innovation is pointless if marginalized people don't have access to already existing technologies or treatments.

Médecins Sans Frontières notes that pharmaceutical companies are faster in filing patents in developing countries than in delivering essential drugs.[77] As the WHO Commission on Intellectual Property, Innovation and Public Health points out in its April 2006 report:

"…current government policies and company strategies including incentive and funding mechanisms, both in developed and developing countries, have not generated sufficient biomedical innovation relevant to the needs of most developing countries. New, and even existing, treatments remain unavailable and unaffordable to those who need them."[78]

Consider, for example:

- One third of the world's population lacks regular access to **essential medicines**. In parts of Africa and Asia, this figure rises to more than half the population.[79]

Médecins Sans Frontières notes that pharmaceutical companies are faster in filing patents in developing countries than in delivering essential drugs.

Box 3: Health in the Millennium Development Goals

Goal 1: Eradicate Extreme Poverty and Hunger:

(Target 2) Halve between 1990 and 2015 the proportion of people who suffer from hunger.

Goal 4: Reduce child mortality:

(Target 5) Reduce by two-thirds, between 1990 and 2015, the under-five mortality rate.

Goal 5: Improve Maternal Health:

(Target 6) Reduce by three-quarters, between 1990 and 2015, the maternal mortality ratio.

Goal 6: Combat HIV/AIDS, Malaria and Other Diseases:

(Target 7) Have halted by 2015 and begun to reverse the spread of HIV/AIDS. (Target 8) Have halted by 2015 and begun to reverse the incidence of malaria and other major diseases.

Goal 7: Ensure Environmental Sustainability:

(Target 10) Halve by 2015 the proportion of people without sustainable access to safe drinking-water and sanitation.

(Target 11) By 2020 to have achieved a significant improvement in the lives of at least 100 million slum dwellers.

Goal 8: Develop a Global Partnership for Development:

(Target 17) In cooperation with pharmaceutical companies, provide access to affordable essential drugs in developing countries.

Adapted from http://www.who.int/mdg/goals/en/

"Every year, more than 14 million people die from treatable infectious diseases. They are dying because medicines are too expensive, no longer produced, increasingly ineffective, highly toxic, or are non-existent."

– Médecins Sans Frontières, "Neglected Diseases: Forgotten Lives," ALERT, Spring 2003

- There is a "fundamental mismatch" between human needs and scientific innovation.[80] The vast majority of commercial drugs are not relevant to tropical diseases. Only 1 percent of the drugs reaching the market between 1974 and 2004 were specifically developed for tropical diseases or tuberculosis.[81]
- Health, poverty and the environment are inextricably linked. According to WHO, unhealthy environments (unsafe drinking water, poor hygiene and other environmental factors) cause nearly one-third of all death and disease in developing countries.[82] Infectious diarrhea kills 1.8 million people per year – mostly children. 88% of the **global burden** of infectious diarrheal disease is caused by unsafe water supply, sanitation and hygiene.[83]
- The global South accounts for over 80% of the world's population, but only 10% of global drug sales. In 2005, Africa accounted for 1.1% share of the global pharmaceutical market. (North America, Europe and Japan accounted for 86% of the global pharmaceutical market.)[84]

Today, formal health care systems in the global South are largely dependent on medical innovation and technologies that are designed primarily to address health markets in OECD countries. Medical R&D in OECD countries is based first and foremost on the pursuit of pharmaceutical industry-led profit, not human needs and development. Ninety percent of the world's health R&D is devoted to conditions that affect just 10% of the population. For example, malaria currently accounts for 3.1% of the **global disease burden**, but only 0.3% ($288 million) of health-related R&D investment. If malaria R&D were funded at the average rate for all medical conditions it would receive over US$ 3.3 billion per annum – more than 10 times the funding it currently receives.[85]

But it is misleading to suggest that the pharmaceutical industry is an engine of innovation for public health in OECD countries. In recent decades, the pharmaceutical industry's capacity to innovate has declined sharply. It is often government and university labs that conduct the most innovative research, which is later acquired by big pharmaceutical firms.[86] In the US, at least a third of drugs marketed by major drug companies are licensed from universities or small biotech companies.[87] After decades of mergers and acquisitions, the pharmaceutical industry is consolidated in the hands of fewer, larger corporations. In 2004, the world's 98 leading drug companies had combined sales of $415 billion; the top 10 companies accounted for almost 59% of the global market share.[88] Instead of developing new compounds, companies are making minor modifications to existing drugs and taking advantage of industry-inspired government policies that allow companies to extend patentability of profitable drugs. For example, of the 78 drugs approved by the US Food & Drug Administration in 2002, only seventeen contained new active ingredients, and only seven were classified by FDA as improvements over existing drugs.[89] The other 71 drugs were "me-too" drugs

– variations of old drugs or deemed no better than products already on the market. Companies are also thwarting the development of cheaper generics – often by paying generic manufacturers to delay the sale of a competing product.[90]

Drug companies typically try to justify their high prices by pointing to their large R&D costs. In reality, drug companies spend far more on "marketing and administration" than on R&D or manufacturing costs. Health researcher Marcia Angell estimates that big pharma's marketing expenditures in 2001 were $54 billion – or 30 percent of the industry's $179 billion revenues.[91] That includes, for example, direct-to-consumer advertising; free drugs samples for doctors; the cost of employing 88,000 sales representatives to visit doctor's offices; gifts to doctors; advertising in medical journals; and marketing and promotion masquerading as "educational" expenses.

The past decade has seen growing controversy over the role of monopoly patents in making drugs unaffordable for poor people and creating barriers to access to life-saving medicines. In 1994 the creation of the World Trade Organization (WTO) and its agreement on Trade-related Aspects of Intellectual Property Rights (TRIPs) mandated that developing countries adopt pharmaceutical patents. At the insistence of South governments, the WTO's 2001 Doha Declaration on the TRIPS Agreement and Public Health re-affirmed the right of governments to use compulsory licensing to facilitate access to cheaper medicines through import or local production, and exempted least developed countries from granting and enforcing pharmaceutical patents until 2016.[93] But the safeguards affirmed in Doha have not been realized and are rapidly eroding as rich governments pursue bilateral trade deals that impose more stringent patent laws above the WTO requirements, undermining the Doha Declaration. The US government, for example, is vigorously promoting bilateral and regional trade agreements that obligate poor countries to recognize "TRIPs-plus" – provisions that aim to prolong big pharma's patent monopolies and limit the use of compulsory licensing and access to cheaper generic drugs.[94]

Analysts note that nanotech-enabled drugs will play a role in securing and extending exclusive monopoly patents on existing drug compounds. According to one industry analyst, "nanotechnology-enabled drug delivery systems have proven to be a weapon against generics" because novel reformulations at the nano-scale may allow an existing compound to qualify as a New Chemical Entity. "This may increase profitability, expand a firm's intellectual property estate, and discourage competition during a drug's most valuable years," according to NanoMarkets.[96] Under this business-as-usual scenario, nanotech's medical innovations are likely to further concentrate the power of the pharmaceutical industry and have little relevance for addressing health and poverty in marginalized communities.

Companies developing high-tech

The past decade has seen growing controversy over the role of monopoly patents in making drugs unaffordable for poor people and creating barriers to access to life-saving medicines.

The safeguards affirmed in Doha have not been realized and are rapidly eroding as rich governments pursue bilateral trade deals that impose more stringent patent laws above the WTO requirements.

The market introduction of nanomedicines is beginning at the same time that out-sourcing of clinical drug trials to the global South is accelerating.

"If you prevent countries from using generic drugs, you are creating a concrete obstacle to providing access to drugs. You are promoting genocide, because you're killing people."

– Pedro Chequer, the head of Brazil's national AIDS program[95]

and costly human performance enhancements may seek to win acceptance for them by touting them as "therapies" to benefit poor people in the developing world. The more likely scenario is that human performance enhancement will increase disparities between the rich and poor, both within and between the North and the South. (See pp. 14–21.)

The market introduction of nanomedicines is beginning at the same time that out-sourcing of clinical drug trials to the global South is accelerating.[97] Ironically, millions of patients in developing countries may finally get access to big pharma's drugs – by serving as human guinea pigs for new and experimental treatments. By 2010 there will be an estimated two million people in India on clinical trials – the vast majority of whom are likely to be poor and illiterate.[98] In 2005, the Indian government revoked its requirement that drugs must be proven safe in trials conducted in the country of origin – prior to being tested on Indian people.[99] *NanoBiotech News* notes that, because there are fewer regulatory hurdles, some nanobiotech companies are conducting early stage clinical trials outside the US and Europe.[100] If this trend continues, the global South may become the early testing ground for nanotech-enabled drugs and devices.

Essential Medicines

The World Health Organization (WHO) defines essential medicines as those that satisfy the priority health care needs of the population.[101] In 1975 the World Health Assembly called on WHO to help member states identify and procure essential medicines, assuring safety, good quality and cost effectiveness. WHO's first essential drug list (now called essential medicines list [EML]), published in 1977, was described as a "peaceful revolution in international public health."[102] The list established the principle that some medicines are more useful than others – and that many essential medicines are often inaccessible to people who need them. Today, most countries maintain national lists of essential medicines. The lists are important because they guide public sector attempts to procure and supply medicines, as well as programmes that reimburse medicine costs, medicine donations and local medicine production.

Over the past 29 years, essential medicine policies have been widely adopted by NGOs, non-profit aid agencies and intergovernmental organizations. But from the beginning, the pharmaceutical industry has opposed the concept of EMLs as an interference with market forces and a threat to private sector operations.

In theory, "essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality, and at a price the individual and the community can afford."[103] But the reality, of course, is far different. There is grave inequity in access to essential medicines even when "access" is defined in the most modest terms – WHO understands access to mean the percentage of

the population able to procure at least 20 essential medicines, which are continuously available and affordable at a health facility or medicines outlet, within *one hour's walk from the patients' home.*[104]

In 1988, WHO published a report on *The World Drug Situation*, which estimated that between 1.3 and 2.5 billion people had little or no regular access to the most essential drugs. When WHO published its follow-up report (called *The World Medicines Situation*) 16 years later, that number was virtually unchanged, though it represented a smaller percentage of the global population – 30%, down from 37%.[105] In four out of the six WHO regions (totaling 183 countries), more countries have very low to medium access to essential drugs (<50-80%) than have medium to very high access (81->95%). For example, out of the 35 countries in the Americas region, 21 have very low to medium access; 14 have medium to very high access.

The following table compares Africa's access to EMs as indicated in the first WHO global medicines report from 1988 and the follow-up report in 2004. According to WHO, 47% of Africa's population does not have access to essential medicines. Out of 45 countries, 16 showed no improvement or a deterioration of access to EMs from the mid-1980s to the late 1990s; all but one of those 16 have very low access to EMs.

There is grave inequity in access to essential medicines even when "access" is defined in the most modest term.

Table 3: Percentage of Populations in African Countries with Regular Access to Essential Medicines

	World Drug Situation, 1988 (Data from 1986-87)	**World Medicines Situation,** 2004 (Data from 1999)	No Change, Decrease or Access Very Low (<50%)
Algeria	60-90%	>95%	
Angola	<30%	<50%	√
Benin	<30%	50-80%	
Botswana	60-90%	81-95%	
Burkina Faso	30-60%	50-80%	
Burundi	30-60%	<50%	√
Cameroon	<30%	50-80%	
Central African Republic	<30%	50-80%	
Chad	<30%	<50%	√
Comoros	60-90%	81-95%	
Congo	30-60%	50-80%	
Côte d'Ivoire	<30%	50-80%	
Democratic Republic of the Congo	n.a.	n.a.	
Djibouti	60-90%	50-80%	
Egypt	60-90%	81-95%	
Equatorial Guinea	<30%	<50%	√
Eritrea	n.a.	50-80%	
Ethiopia	30-60%	50-80%	
Gabon	60-90%	<50%	√
Gambia	60-90%	81-95%	
Ghana	30-60%	<50%	√
Guinea	<30%	81-95%	
Guinea-Bissau	30-60%	<50%	√
Kenya	60-90%	<50%	√
Lesotho	60-90%	50-80%	√
Liberia	<30%	<50%	√
Libyan Arab Jamahiriya	60-90%	>95%	
Malawi	30-60%	<50%	√
Mali	<30%	50-80%	
Mauritania	<30%	50-80%	
Mauritius	60-90%	>95%	
Morocco	30-60%	50-80%	
Mozambique	30-60%	50-80%	
Niger	30-60%	50-80%	
Nigeria	<30%	<50%	√
Rwanda	<30%	<50%	√
Senegal	<30%	50-80%	
Sierra Leone	30-60%	<50%	√
Somalia	<30%	<50%	√
Sudan	<30%	<50%	√
Togo	30-60%	50-80%	
Tunisia	30-60%	50-80%	
Uganda	30-60%	50-80%	
Zambia	30-60%	50-80%	
Zimbabwe	30-60%	50-80%	

"Pro-Poor" Nano?

Two products currently under development are frequently cited as examples of nanotech's potential to address major health problems in the developing world: 1) an engineered microbe that synthesizes **artemisinin,** which is a potent anti-malarial drug; 2) a vaginal microbicide based on nanoscale molecules that is designed to protect women from HIV/AIDS and sexually-transmitted diseases. Both cases are highlighted below.

Nano-scale Engineering to Produce Anti-malarial Drug

Engineering microbes to produce an inexpensive anti-malarial drug is the *cause célèbre* of **synthetic biology**, a convergence of biotechnology and engineering to build biological systems in the laboratory to perform specific tasks. Malaria afflicts 300-500 million people and kills more than one million people per annum (58% of malaria cases occur among the poorest 20% of the world's population – mostly young children living in Africa).[106]

With support from the Bill and Melinda Gates Foundation, Jay Keasling, professor of chemical engineering at the University of California Berkeley and director of its Center for Synthetic Biology, is building a microbial chemical factory to manufacture artemisinin – a powerful anti-malarial agent.

Artemisinin, a natural product extracted from the leaves of the sweet wormwood plant *Artemisia annua*, has successfully treated all known strains of malaria. The Chinese have used the wormwood shrub as a medicinal plant for over 2,000 years. Naturally-derived artemisinin is currently in short supply, although some experts believe it is technically possible to cultivate sufficient amounts of wormwood to produce enough artemisinin to treat all the malaria patients in the world.[107] Chemical synthesis of the drug is slow and costly.[108] In 2004, Keasling's Berkeley lab and his start-up company, Amyris, together with the non-profit Institute for OneWorld Health, received a 5-year, $43 million grant from the Bill and Melinda Gates Foundation to develop a microbe-derived version of artemisinin. Keasling's lab is now engineering the metabolic pathways of an engineered yeast (*Saccharomyces cerevisiae)* to produce the intermediate products that are needed to produce artemisinin.[109] The lab has already produced artemisinic acid – one step away from producing artemisin itself. According to Keasling, the next step will require chemistry, and the end product won't be coming soon – it could be 10 years before microbes can churn out enough artemisinic acid to address global malaria.[110] If researchers need another decade to succeed, how much will the synthetic biology approach to producing artemisinin ultimately cost?

If engineered microbes can successfully produce a treatment for malaria, will the product be accessible and/or affordable? UC Berkeley has given Amyris and OneWorld Health a royalty-free license to develop the anti-malarial treatment. Keasling says

Engineering microbes to produce an inexpensive anti-malarial drug is the cause célèbre *of synthetic biology, a convergence of biotechnology and engineering to build biological systems in the laboratory to perform specific tasks.*

If engineered microbes can successfully produce a treatment for malaria, will the product be accessible and/or affordable?

A simple, low-cost technology already exists (condoms) that is easier to distribute and store – but condoms remain in short supply. For example, in 2003, donor contributions paid for the equivalent of one condom a year for each man of reproductive age living in the developing world.

that Amyris will produce the drug at cost, and the non-profit drug company, OneWorld Health, would perform the work necessary to clear regulatory hurdles. Amyris hopes to use the same technology platform to produce far more lucrative drugs. According to the company's website: "The Amyris team of scientists and engineers is now poised to commercialize pharmaceuticals and other high value, fine chemicals taken from the world's forests and oceans by making these compounds in synthetic microbes."[111]

Nevertheless, researchers may find themselves hamstrung by a complex web of intellectual property claims on both processes and products related to the production of artemisinin – that could obligate them to negotiate royalties and pay licensing fees to multiple patent holders. Recall, for example, the case of biotech's much-heralded, vitamin-A fortified "Golden Rice" developed to address nutrient deficiencies of poor people in the South. Stymied by some 70 conflicting patent claims, the publicly-funded Golden Rice researchers surrendered the project to multinational agrochemical giant AstraZeneca (now Syngenta) in 2000. The controversial Golden Rice has yet to be commercialized.

VivaGel – Downsizing Microbicides

"Microbicides" refer to a range of compounds now under development that aim to reduce or prevent the transmission of HIV and other sexually transmitted diseases when applied topically. Worldwide over 7,000 women become infected with HIV every day. Some women's health advocates are promoting the development of microbicides because they could put safe, affordable and accessible protection into the hands of women.[112] Microbicides are not yet commercially available, but almost 20 are in clinical trials.

One of the vaginal microbicides in human trials, Starpharma's "VivaGel," is based on nano-scale molecules called **dendrimers** – synthetic, three-dimensional molecules with branching parts. The active ingredient in VivaGel works like molecular velcro – inactivating HIV and genital herpes viruses by binding with receptors on the virus's surface and preventing it from attaching to the host cells it is trying to infect.[113]

VivaGel is being developed as a topical microbicide that has the potential to prevent the transmission of HIV and other sexually transmitted diseases (STDs) when applied to the vagina prior to sexual intercourse. In animal studies, the main ingredient in VivaGel has also acted as an effective contraceptive.[114] If Vivagel can protect against STDs and pregnancy, market analysts see it competing with the condom market.[115] Vivagel is the first dendrimer to go through the FDA process and is now being tested around the world in various populations.[116]

In 2005 the US National Institutes of Health (NIH) awarded Starpharma (based in Melbourne, Australia) US$20.3 million to support the development of VivaGel for the prevention of HIV.

In April 2006 the US NIH announced it would fund a clinical trial to test the use of VivaGel in the

prevention of genital herpes.

Ultimately, will vaginal microbicides be safe, affordable and accessible to those who need them most? (Sex workers in Nigeria are now applying lime juice to their vaginas in an attempt to protect themselves from contracting HIV – will they have access to high tech protection in the near future?[117]) Some women's health advocates point out that a simple, low-cost technology already exists (condoms) that is easier to distribute and store – but condoms remain in short supply. For example, in 2003, donor contributions paid for the equivalent of one condom a year for each man of reproductive age living in the developing world.[118]

According to Eldis (Institute of Development Studies, Essex) the

Box 4: The "Grand Challenge" Approach to Global Health: Is it Working?

According to *Science*, over the past seven years more than $35 billion have been spent on fighting diseases that disproportionately affect the poor.[1] A big chunk of that money has come from the disproportionately rich. Since 1999, the world's richest man, Bill Gates – through the Bill and Melinda Gates Foundation – has given away $6 billion, which roughly equals the programme budget of WHO for the same period.[2] In June 2006, über-wealthy investor Warren Buffet (by some accounts the world's second richest man) announced plans to hand over about $31 billion of his $44 billion to the Gates Foundation – a giveaway that will eventually double the charity's assets.[3] According to *The Economist*, it is rapid wealth-creation – there are now 691 billionaires in the world, up from 432 a decade ago – and uneven distribution of wealth that largely explain the current enthusiasm for deep-pocketed philanthropy.[4]

Wealthy donors often align themselves with blockbuster, global campaigns that involve governments, corporations and foundations in Public-Private Partnerships (PPPs). The goals can be as ambitious as the involvement is broad – "Making Poverty History" or "Roll Back Malaria," for example. PPPs are seen as a way to accomplish what the P-Public is unable to do and the P-Private has no incentive to do. Ten years ago, there was not a single PPP devoted to the development of "**orphan drugs**" – medicines to treat diseases with little or no financial profit potential – and today there are more than 63 drug development projects aimed at diseases prevalent in the global South.[5] The prospects for profit from the sale of orphan drugs hasn't changed, but well-endowed philanthropical foundations and, to a lesser degree, governments have offered pharmaceutical companies a deal too sweet to refuse: Foundations and governments provide cash and companies provide drug development know-how and infrastructure for clinical trials. According to *Science*, big pharma's benefits from the "no profit-no loss" model include a "good public image and an introduction to developing-country markets and researchers who might help them elsewhere."[6]

"If there's one universal, time-tested truth in the global battle against infectious diseases, it is this: easier said than done…The revolution that is sweeping through the global health effort has clearly brought more money, tools, creative ideas, and momentum than ever before. But the goal – narrowing the gap between aspirations and actions – remains a staggering challenge."

– Jon Cohen, "The New World of Global Health," Science, 13 January 2006

The development of a microbicide which is replicable, sustains a good shelf life and is attractive to users will require an estimated US$600 million over the next ten years.

development of a microbicide, which is replicable, sustains a good shelf life and is attractive to users, will require an estimated US$600 million over the next ten years.[119] In theory, microbicides could give women greater power to protect themselves against HIV without having to rely on partner cooperation. But gender inequality is the root problem, and unless that is addressed, a new technology cannot offer a simple solution. Some women's health advocates believe that money could be better spent on programs to empower women, to increase their income and ability to control their own lives. There are also numerous health and safety issues surrounding the development of microbicides, especially in the global South where poor living conditions can complicate safe and effective use. Based on historical patterns, there is concern that political pressures to approve effective microbicides could compromise rigorous testing and that vulnerable populations of women will be used as guinea pigs (i.e., early clinical trials of one microbicide [not Starpharma's] tested on sex workers actually increased the incidence of HIV infection in women).[120]

"VivalGel" is a proprietary technology, and Starpharma's self-described business strategy "is to create value from dendrimer nanotechnology by utilising its IP through product development, licensing and partnerships."[121] Starpharma holds rights to three broad-based US patents in the dendrimer pharmaceutical area. In addition, Starpharma holds a 33% interest in Dendritic NanoTechnologies, Inc. (DNT), which holds more patents on dendrimer technology than any other company. (Dow Chemical Co. also holds a 33% equity position in DNT.)

The table on page 35 provides details on seven global health initiatives – all of them PPPs. Though statistics related to the incidence of disease in the global South can only be described in the grimmest terms – average life expectancy *has gone down* in 38 countries since 1999, due primarily to the spread of HIV;[122] 2 million children die every year from vaccine-preventable diseases;[123] a child dies of malaria every 30 seconds in sub-Saharan Africa;[124] more than 8 million people become sick with infectious tuberculosis every year[125] – it would be unfair to dismiss any one programme as a categorical failure, given the overwhelming challenges and the relatively early stage of the projects. Only one initiative is more than a decade old and five are less than five years old. (The possible exception is the Roll Back Malaria Programme, which the *British Medical Journal* described as a "failing health initiative" in 2004 due to its inability to make available malaria-fighting tools – bed netting, insecticides, artemisinin-based medicines – to the poorest communities.[126])

On the other hand, it would be disingenuous to declare any of the programmes a categorical success. None of the initiatives is above critique, some more fraught with problems than others. In June 2006 *The New York Times* shined a spotlight on some of the failures related to the fight against malaria: The Global Fund has yet to deliver

one of the 1.8 million mosquito-nets it promised to Uganda in 2004; the World Bank has no staff members working on malaria though in 2000 it pledged to halve malaria deaths in Africa; only 8% of the US Agency for International Development's (USAID) 2004 malaria budget went to medicines, nets and insecticides – the bulk was spent on consultancy fees and meetings.[127] Criticisms of high-profile health initiatives in general include mismanagement (outright corruption in some cases), duplication of efforts, inefficiency, short-sightedness and a lack of global "architecture" capable of bringing different efforts together.[128] With enthusiasm growing for the potential of nanomedicine to solve some of the world's grandest health challenges, it is important to stress that no one innovation will make these structural problems disappear.

Table 4: Current Global Health Initiatives

Initiative	Focus	Year Launched	Donors	Pledged, Committed or Spent Funds, $
Grand Challenges in Global Health Initiative[1]	Applying science & technology to health problems of developing world	2003	Gates Foundation, Wellcome Trust, the Canadian Institutes of Health Research and the Foundation for the National Institutes of Health (US)	481.6 million
Global Fund to Fight AIDS, Tuberculosis and Malaria	Financing treatment and prevention	2002	Governments, Gates Foundation, Hewlett Foundation, UN Foundation, Novartis, Statoil and others	8.6 billion
Global Alliance for Vaccines and Immunization (GAVI)	Financing and developing of childhood vaccines	1999	WHO, UNICEF, World Bank, NGOs, Gates Foundation, governments, vaccine industry (Wyeth, Chiron, Berna, GSK, Merck, Sanofi) and others	3 billion
Various PPPs for Drug, Vaccine, Diagnostic, Microbicide Development	Developing treatments, vaccines, diagnostics	n/a	Various governments, foundations, philanthropists, corporations	1.2 billion
Multi-Country HIV/ AIDS Program	Financing scale-up of existing gov't and community prevention and treatment efforts	2000	World Bank	1.1 billion
International AIDS Vaccine Initiative	AIDS vaccine R & D	1996	World Bank/Global Forum for Health Research governments, Becton, Dickinson and Co., Gates Foundation, Continental Airlines, Deutsche AIDS-Stiftung, DHL, Google, Otto Haas Charitable Trust #2, Pfizer, Rockefeller Foundation, Until There's a Cure Foundation and others	>100 million
Roll Back Malaria Partnership	Treatment and prevention	1998	Governments, World Bank, UN agencies, academic institutes, NGOs, corporations, individuals	~150 million[2]

Sources: *Science* 13 January 2006, p. 163; ETC Group

Applications of Nanomedicine

(drug delivery, therapy, imaging and diagnostics)

"The promise of nanotechnology for cancer imaging is that we have little doubt that it will lead to far more sensitive and accurate detection of early stage cancer…These efforts will blur the boundaries of what we call detection and what we call therapy."

– Adrian Lee, professor of medicine, Baylor College of Medicine[130]

The potential applications of nanotechnology in medicine are vast. In this section we provide examples that reflect the most intensive areas of current nanomedicine R&D (or commercial products) – targeted drug delivery, nano-enabled therapies, imaging and diagnostics. We have chosen not to provide a laundry list of possible applications (there are hundreds) but instead offer a few illustrations of nanomedicine applications in each area. It should be noted that drug delivery, imaging and diagnostics are not always distinct sectors. In cancer research, for example, the ultimate goal is to develop multifunctional nano-scale devices that act as both imaging agent and anticancer therapy.[129]

1. Targeted Drug Delivery

One of the most highly publicized areas of nanomedicine research involves gold nanoshells to detect and treat cancerous tumors.

Gold Nanoshells: One of the most highly publicized areas of nanomedicine research involves gold nanoshells to detect and treat cancerous tumors. Here is a case where detection and therapy overlap: The nanoshells are imaging agents that also function as therapeutic agents. Though the idea of nanoshells goes back to the early 1950s, their creation was put off several decades until it was possible to engineer particles on the nano-scale.[131] Naomi Halas of Rice University (Houston, USA) developed gold nanoshells in the 1990s. She and colleague Jennifer West, also of Rice, formed start-up Nanospectra Biosciences, Inc. in 2002. Since then, the company has received over $5 million in funding to develop medical uses of gold nanoshells (including more than $3 million in federal money).[132] Data from human trials is expected in early 2007.[133]

Halas's nanoshells are particles of silica (glass) completely coated with gold, made up of a few million atoms. They can be produced in a range of sizes, with diameters smaller than 100 nm to as large as several hundred nm. The manufacture of nanoshells requires nano-scale engineering techniques in order to fine-tune the nano-scale thickness of the gold coating so that it will exhibit the desired optical properties. When injected into the blood stream, they naturally congregate at tumor sites – so no additional targeting is necessary. In order to feed their growth, tumors create many, many blood vessels very quickly, so the vessels are often defective, allowing the nanoshells to slip through vascular "leaks" and gain access to the tumor. Detecting and targeting tumors by exploiting their surrounding vascular defects is known as "enhanced permeability and retention," or EPR, effect.

Halas describes a nanoshell as "essentially a nanolens" that captures light and then focuses it around itself.[134] By manipulating the size of the nanoshells – both the size of the glass core and its gold coating – it's possible to change the way they absorb light. The goal in cancer detection and therapy is to "tune" the nanoshells to interact with near-infrared light (NIR).[135] When exposed to NIR,

the nanoshells act like a swarm of fireflies and light up the area where they've congregated (i.e., tumor sites). Once the nanoshells have completed their imaging tasks, they become therapeutic agents. Shining a near-infrared laser on the tumor site from outside the body (light can travel through tissue more than 10 cm), the nanoshells absorb the light and focus it on the tumor. The area around the nanoshells heats up and the tumor "cooks" until it is ablated (dissipated). It's not so different from the familiar childhood science experiment: The nanoshell functions as the magnifying glass, the laser is the sun and the tumor heats up like the blade of grass.

In 2005, Halas described compelling results from nanoshell cancer treatment in mice:

"Once [the nanoshells] are in place, infrared light is shined through the skin and down into the tumor site. It's a very simple handheld laser, and it's only for three minutes… In mouse studies, we were able to observe complete remission of all tumors within 10 days. There were two control groups of mice, and their tumors all continued to grow very drastically until their end. But the mice that were treated with nanoshells, they survived the study…there was 100 percent survivability, and the survivability persisted. That test was done in 2003. It's almost two years later. So it looks like most of those mice will be dying of old age."[136]

Halas points out that the nanoshells leave no "toxic trail" in the body the way conventional chemotherapeutic agents do. Nanospectra's web site states that "long-term studies have not indicated any toxicity or effect on the immune system."[137] These claims will have to be closely scrutinized, as nanoshells will likely take up permanent residence in the body – it's not clear how or if the body could excrete them.

2. Therapeutic Nanoparticles

Nano's Silver Bullet? Medical products incorporating nano-scale silver are among nanotech's early commercial successes. Although the antimicrobial properties of silver have been known for millennia, the increased surface area of engineered silver nanoparticles (1-100 nm) makes them more chemically reactive and enhances their therapeutic properties.

Medical products incorporating nano-scale silver are among nanotech's early commercial successes.

Nucryst Pharmaceuticals (a subsidiary of Westaim Corporation) manufactures dressings for wounds and burns that are impregnated with nano-scale silver to fight infection and inflammation. Silver kills bacteria and viruses by preventing electron transport in microbes and by impairing cell replication when it comes in contact with DNA. Silver ions (atoms that have an electrical charge due to a change in the number of electrons) also disrupt microbial structures and functions.[138] The downside is that high levels of silver ions released over extended periods of time can kill cells as well, so exposure must be carefully controlled.[139]

Municipal water treatment specialists are wondering if nanoscale silver in washing machines could cause serious problems if silver particles are discharged in wastewater and kill the plankton, disrupting the food chain.

Smith & Nephew, one of the world's largest medical equipment firms, sells Nucryst's silver-coated wound dressings in 30 countries under the name "Acticoat." The demand for antimicrobial dressings is growing because many bacteria are rapidly

The potential advantage of using quantum dots for imaging inside the human body is that they offer the "ultimate detection sensitivity" – a single protein tagged with a fluorescent quantum dot can be tracked inside a living cell.

becoming resistant to antibiotics. Smith & Nephew claims that Acticoat is effective against 150 pathogens including some resistant microorganisms.[140]

Johnson & Johnson, Bristol-Myers Squibb and Medline Industries are among the other companies commercializing medical products based on nano-scale silver. But wound dressings are just the beginning. Since hospital-related bacterial infections are estimated to be the fifth-leading cause of death in the United States, companies are looking at the use of nano-scale silver as a coating on surgical tools, in bed sheets and hospital curtains.[141] In December 2005 the US Food & Drug Administration granted approval for a catheter (a tube for transporting liquid) coated with antimicrobial silver for implantation into the human body.[142]

Nano-scale silver coatings are also being used as antimicrobials on consumer products such as refrigerator linings, brooms, food storage containers and clothes. "SmartSilver" antimicrobial socks are sold to soldiers in US military stores and researchers are developing fabrics with silver-nanoparticle coatings described as "self-cleaning."[143] A new washing machine marketed by Samsung (SilverCare) injects silver ions into the wash and rinse water. Samsung claims that the silver ions penetrate fabrics and kill bacteria without the need for hot water or bleach. Municipal water treatment specialists are wondering if nanoscale silver in washing machines could cause serious problems if silver particles are discharged in wastewater and kill the plankton, disrupting the food chain.[144] Following a request by the National Association of Clean Water Agencies in early 2006, the US Environmental Protection Agency is considering, as of June 2006, whether to review and classify products containing silver nanoparticles as pesticides – capable of killing plant life.[145]

3. Nanoparticles for Biomedical Imaging and Diagnostics

"Quantum dots" are semiconductor nanoparticles that have unique optical and electrical properties. When exposed to light, these nanoparticles emit distinctly different colors depending on their size. (The smaller the quantum dot, the brighter the color.) Although fluorescent dyes have been used for decades in the human body for biomedical imaging (to track the effects of cancer drugs, for instance), they are often imprecise and only visible for short time periods. Biomedical researchers are hoping that fluorescent quantum dots will provide a brighter, more precise and longer-lasting alternative. Fluorescent quantum dots are already being used for tracking or labeling biological material *in vitro* and *in vivo* in animals (other than humans) for research purposes. Quantum dots can be injected into cells or attached to proteins in order to track, label or identify specific biomolecules. For biomedical researchers, the potential advantage of using quantum dots for imaging inside the human body is that they offer the "ultimate detection sensitivity" – a single protein tagged

with a fluorescent quantum dot can be tracked inside a living cell.[146]

Engineered quantum dots are already being employed in electronics (display panels and flat-screen televisions) but they have not yet been approved for therapeutic/diagnostic purposes, largely because of concerns about potential toxicity. Current research suggests that, "under certain conditions QDs may pose environmental and human health risks."[147] The inner core of most quantum dots is made of cadmium and selenium, which are known to cause acute and chronic toxicities in vertebrates at low concentrations.

In an attempt to make quantum dots safe and biologically compatible, their core and inner shell are encapsulated in a bioactive coating that "functionalizes" them – makes them suitable for molecular imaging or drug delivery, for example. If the outside coating degrades, however, it could expose the toxic core. Quantum dots can stay inside cells for weeks or months – but virtually nothing is known about how these nanoparticles metabolize inside the body or their routes of excretion.[148]

A recent toxicologic review of quantum dots by Duke University (North Carolina, USA) researcher Ron Hardman concludes that it won't be easy to determine which quantum dots pose problems because – as with nanoparticles generally – even those that are chemically similar can have markedly different physical and toxicological characteristics. With quantum dots, size, shape and the composition of both metal core and outer shell coating can be a factor in determining toxicity. As a result, "each QD type will need to be characterized individually as to its potential toxicity."[149]

Carbon Dots? Researchers at Clemson University (South Carolina, USA) have recently developed a new type of quantum dot made from carbon that they believe could be more benign than particles composed of cadmium, **selenium** or lead.[150] When carbon nanoparticles are covered with special polymers, they glow brightly when exposed to light. Researchers believe that the photoluminescence may be due to the presence of energy-trapping "pockets" or holes on their surface.

DNA Detector: Nanosphere, Inc. (Illinois, USA) has developed an ultrasensitive DNA and protein detector system – two instruments, each about the size of a desktop computer – that the company says is "orders of magnitude more sensitive than other detection techniques" and "will completely change the way the world looks at diagnostics."[151] Based on blood or saliva samples, the company's DNA detector, dubbed "Verigene," automates the identification and analysis of nucleic acids and proteins. The DNA detector will reveal, for example, if a patient has a genetic mutation that makes them genetically predisposed to a disease or likely to develop blood clots during surgery. The company claims that its product can detect proteins in concentrations a thousand times lower than current methods – allowing detection of a protein released in the body during a heart attack, or even someday a

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"Virtually any disease that results from malfunctioning, damaged or failing tissues may be potentially cured through regenerative medicine therapies."

– US Department of Health and Human Services, *2020: A New Vision, A Future for Regenerative Medicine*. 2005[153]

Nanotechnology will play a key role in tissue engineering because it operates on the molecular scale and is capable of integrating both biological and non-biological materials.

protein associated with early-stage Alzheimer's.

The Verigene system uses different techniques to detect DNA and proteins, but both systems make use of gold nanoparticles to create highly selective and sensitive probes. When the probes are combined with a sample, they target and bind only with the complementary genetic construct. The system is capable of identifying multiple genetic markers with a single test.

Medical Nanosensors: Researchers at the University of Illinois are developing a tiny, implantable device that would allow diabetics to monitor glucose levels without drawing blood.[152] The sensors are made of carbon nanotubes – cylinder-shaped molecules of pure carbon – that naturally fluoresce when illuminated by infrared light. The goal is to develop a sensor that can be implanted just under the skin and will send an optical signal when illuminated by an infrared light. In essence, the more glucose present in the body, the brighter the nanotubes would glow. Implantable glucose sensors are just the beginning. Researchers hope someday to develop other sensors to detect a wide range of biochemicals such as hormones, cholesterol and drugs.

4. Tissue Engineering/Implants

Regenerative medicine has been described as "the vanguard of 21st century healthcare" because it offers the promise of replacing or regenerating tissues and organs.[154] Researchers are already employing nano-scale technologies in tissue engineering, with the goal of creating fully biological or bio-hybrid tissues and organs *in vitro* (in the laboratory) that can be safely implanted in the human body. A 2005 report prepared by the US Department of Health and Human Services enthusiastically predicts that the worldwide market for regenerative medicine will be $500 billion by 2010 (this figure is not limited to nano-enabled regenerative medicine).[155]

Tissue Engineering: Nanotechnology will play a key role in tissue engineering because it operates on the molecular scale and is capable of integrating both biological and non-biological materials. For example, researchers are using self-assembling nano-structures to create artificial collagen (that is, the connective tissue proteins that are the main protein component of bones, skin, teeth and tendons). Because collagen proteins are a major structural component in the body's tissues and organs, researchers hope to use nano-structured artificial collagen as the three-dimensional scaffolding that is needed to encourage cell regeneration – for growing specific cells, tissues and even organs.[156]

Researchers are already using this technique to grow bladder tissue.[157] Some 60,000 people in the US are treated for bladder cancer each year, which requires removing portions of their bladder. To replace bladder tissue that has been surgically removed, scientists must first create a biocompatible scaffolding on which the patient's new bladder cells can grow. Researchers at Purdue University are using nanostructured polymers (long chain molecules) that are

biocompatible, biodegradable and flexible to build a three-dimensional scaffold with nanometer-sized bumps across its surface. The nanostructured polymer scaffold is then "seeded" with bladder cells taken from the patient. Because the bladder cells come from the patient who receives the transplant, the new tissue is less likely to be rejected. The cells reportedly grow faster when grown on scaffolding with nanoscale surface features. The hope is that, after being implanted in the human body, the scaffolding will dissolve slowly, leaving intact functional bladder tissue.

In April 2006, researchers reported that the first urinary bladders grown in the laboratory and transplanted in seven children and young adults had been functioning successfully for almost four years.[158] The *Washington Post* described the feat as the Holy Grail of medicine: "the first cultivation of working replacements for failing solid organs in people."[159] The bladder transplants were conducted on an experimental basis, and have not yet received approval from the US Food and Drug Administration. The company that is commercializing the bladder transplant technology, Tengion, has not revealed the estimated cost of the transplant. Transplanting bladders grown from a patient's own cells marks the beginning of the era of "rejuvenation medicine," in which organs that are underperforming – due to disease or old age – can be exchanged for better working models. Some futurists hope to amass a collection of spare parts – including hearts – in anticipation of the body's inevitable decline.[160]

Bone-Grafting Materials: Nano-scale materials are being used to develop synthetic bone replacement materials with improved durability, bioactivity and strength. NanoCoatings Ltd. (Australia) is developing a technology to produce synthetic bone replacement material that could be used for bone-grafting or for bioactive coatings on artificial joints – such as hip and knee replacements and dental implants. The company's bone-graft material, still in early stages of development, is derived from hydroxyapatite – a naturally occurring substance that is also the main mineral component of dental enamel and bone – coated with nano-scale carbonate apatite.[161]

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Nano-enabled medicines and performance enhancement technologies threaten to re-direct scarce medical R&D funds away from essential health needs.

In the current socio-economic context, it is very likely that high-tech, proprietary nano-medicines will be largely inappropriate, inaccessible and unaffordable for marginal communities in the North and the South.

Conclusion

Wrong Prescription? The development of nanomedicine and its impacts on marginalized communities must be understood in a larger social and political context. The fundamental issue – not unique to nanotech – is that new technologies have not provided solutions to complex problems rooted in poverty and social inequities. Nano-enabled medicines and performance enhancement technologies threaten to re-direct scarce medical R&D funds away from essential health needs. Further, the emphasis on high-tech medical interventions threatens to divert attention and resources away from non-medical approaches that address human development. Basic interventions that lead to improved sanitation and housing, nutrition, access to clean water and education – for example – may ultimately lead to far greater advances in human health than cutting-edge medical technologies.

Innovation in nanomedicine is being driven largely from the North to meet the market-driven health needs of OECD countries. Today, the vast majority of medical R&D is determined by profits, not human needs. Although nanotech boosters will point to compelling cases of nanotech R&D that they claim have the potential to address major health needs in the developing world (an engineered microbe that synthesizes a powerful anti-malarial drug and a microbicide to protect women against HIV/AIDS), it is very likely that high-tech, proprietary nanomedicines will be largely inappropriate, inaccessible and unaffordable for marginal communities in the North and the South.

Nanotech R&D devoted to safe water and sustainable energy could be a more effective investment to address fundamental health issues. However, these applications require further study and are beyond the scope of this report.

In the coming years there will be greater emphasis on personalized medicine, and technological convergence will make it theoretically possible to augment the structure, function and capabilities of human bodies and brains. The line between enhancement and therapy will disappear, and ultimately shift society's perception of what is "normal." The emphasis on HyPEs (human performance enhancements) not only threatens to re-direct scarce medical R&D funds away from essential health needs of marginalized people, it will ultimately create an "ability-divide." Like the digital divide, the ability divide will widen the gap between North and South, and between rich and poor everywhere. In the prevailing social and political context, the introduction of pervasive enhancement technologies is likely to result in new groups of marginalized people.

Crucial questions remain unanswered about the health and environmental impacts of nano-scale materials that are currently being used in the development of nanomedicines. Although

advocates promise that nanotech will bring revolutionary advances in medicine – it is also possible that some applications of nanotech could introduce new hazards to human health. The toxicology of engineered nanomaterials is largely unknown, and toxicity data cannot be extrapolated from existing toxicology studies conducted on larger scale particles of the same substance. Recent toxicological studies on the health and environmental impacts of manufactured nanoparticles indicate that there are reasons for concern. And, despite the fact that nano-scale products have already been commercialized (including nanomedicines), no government in the world has developed regulations that address the safety of nano-scale materials.

Because of a growing trend to conduct clinical drug trials in some areas of the developing world, unproven nanomedicines may be tested on people in the global South before they are tested and approved by governments in the North. There are currently no requirements for the labeling of nano-scale materials, and no established definitions or standards for describing them. Given the regulatory vacuum, there is concern that South governments (and people in drug trials) will not be fully informed if nano-scale technologies are involved in domestic drug trials.

Governments must examine how medical R&D priorities are determined and financed, and how innovations are rewarded. Will access to essential medicines be determined by governments or by the drug companies that hold patents on them? At the May 2006 World Health Assembly (WHA), the governing body of the WHO, governments pledged to begin work on a global strategy and framework to support needs-driven, essential health R&D. The new framework will emphasize access to new medical inventions and explore methods of rewarding innovations that do not rely on market monopolies and high prices. The resolution adopted by the WHA is an ambitious step in the right direction.

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Governments must examine how medical R&D priorities are determined and financed, and how innovations are rewarded. Will access to essential medicines be determined by governments or by the drug companies that hold patents on them?

Recommendations

Emerging nano-scale technologies require scientific, socio-economic and societal evaluation in order for governments to make informed decisions about their risks/benefits and ultimate value.

Before rushing to embrace nanomedicine as a technological imperative, society must become fully engaged in a wide discussion about nanotech. Emerging nano-scale technologies require scientific, socioeconomic and societal evaluation in order for governments to make informed decisions about their risks/benefits and ultimate value. As part of a larger process of determining health care priorities, developing nations should become active participants in assessing what role nano-scale technologies could or should play in addressing health needs. To keep pace with technological change, innovative approaches are needed to monitor and assess the introduction of new technologies.

Technology and Diversity: The introduction of high-tech medical technologies can inadvertently push-aside existing, low-technology interventions that may play an important role in public health for some segments of the population. In many developing countries, especially in rural areas, 80% of people depend on traditional health practitioners and traditional medicines.[162] One public health strategy is to focus on improving access to existing knowledge and practices – instead of the proprietary products of imported, capital-intensive R&D. The April 2005 report of the WHO Commission notes: "The possibilities exist for making better use of traditional medicine, by making traditional remedies more widely available, and by applying this knowledge to accelerate the development of new treatments."[163]

Ultimately, society must actively maintain and use a diversity of viable technologies that are socially, economically and environmentally appropriate. If technologies are to be used to address diverse societal needs in diverse cultural contexts, it is important that governments maintain diverse technologies (both old and new) and recognize and encourage indigenous technology innovations that are often overlooked in the face of pressures to accept dominant technology introductions.

Health and Safety of Nanomedicines: In collaboration with civil society and in consultation with scientists, national governments should establish a *sui generis* regulatory regime, based on the precautionary principle, specifically designed to address the unique health and environmental issues associated with nano-scale materials. (This is not a call for a UN nanotech safety protocol, however.) It is crucial that regulatory discussions are not limited to health, safety and environmental issues – they must also include discussion of broader socio-economic impacts, including control and ownership of the technologies and impacts on marginalized peoples.

To make wider evaluations of nano-scale science and technology, including the impacts of intellectual property, ETC Group advises governments to consider establishing a moratorium on

nanotechnology, and all domestic drug trials involving nano-scale materials, until regulations are in place to protect workers, research subjects, consumers and the environment – and until wider social impacts are considered.

Nanotech and Intellectual Property: Intellectual property plays a large role in science and technology development today, and the race to win monopoly control of nanotech's colossal market is underway. Patents on nano-enabled medicines, diagnostics and devices will influence who has access to nanotech innovations, and what price they must pay. Studies are needed to examine the implications of intellectual property and nano-scale technologies for public health. Governments should request that WHO, in consultation with WIPO, initiate studies to examine the special implications of nanotech-related intellectual property on monopoly practices, technology transfer, trade and public health – especially for countries in the global South.

Social and Ethical Implications of Converging Technologies: Although human performance enhancement technologies (HyPEs) may seem distant, research in this field is advancing rapidly and raises far-reaching ethical concerns that should be addressed by governments and civil society. Societal debates about the ethical, social and economical implications of enhancement and life extension are crucial. Governments should request that the Human Rights Commission undertake studies on the implications of technologies converging at the nano-scale, particularly for people with disabilities and other marginalized populations in the global South. Representatives of disability rights and sexual and reproductive health rights organizations, as well as other social movements and civil society should be consulted in this process.

At its next meeting in 2007, the World Health Assembly should request that WHO undertake a full analysis of nanomedicine, nano-scale technological convergence and the potential social and economic impacts of human performance enhancement on marginalized communities. Representatives of disability rights organizations, as well as other social movements and civil society, should be consulted in this process.

Legally-binding, multilateral approach to Technology Assessment: Rather than approaching technology assessment in a piece-meal fashion, governments should also consider longer-term strategies to address the introduction of significant new technologies on an ongoing basis. To break free from the cycle of social disruptions that accompany each new technology introduction, the international community needs an independent body that is dedicated to assessing major new technologies and providing an early warning/early listening system. One possibility is the establishment of an intergovernmental framework called the International Convention on the Evaluation of New Technologies – ICENT). The objective of ICENT would be to create a socio-political and scientific environment for the sound and timely evaluation of new technologies in a participatory

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and transparent process that supports societal understanding and debate, encourages social and scientific innovation and facilitates equitable benefit-sharing. Further, the inter-governmental framework would ensure the conservation of useful, conventional or culturally-distinct technologies and, in particular, promote technological diversification and decentralization. (For details on ICENT, see ETC Group report, "Nanogeopolitics," July/August 2005.)

The process of United Nations negotiations to develop an international agreement such as ICENT would also stimulate high-level and broad societal discussion, and encourage national and regional legislative and institutional initiatives that would complement an international agreement.

Global Dialogue Initiative on Nanotech and the Poor: A current initiative, the "Global Dialogue on Nanotechnology and the Poor: Opportunities and Risks," is supported by the Rockefeller Foundation, the International Development Research Centre of Canada and the UK's Department for International Development.[164] In order for the dialogue to be useful, it must have input from representatives of the global South, and those populations most vulnerable to the disruptive impacts of nano-scale technologies. To insure that multi-stakeholder dialogues examine the potential impacts of nanotech from a diverse group of stakeholders, it is also important that developing country representatives from the disability, health and workers' rights communities and civil society participate.

Appendix: Nanomedicine Glossary

Artemisinin – a natural product extracted from the leaves of the sweet wormwood plant that has successfully treated all known strains of malaria. Using **synthetic biology**, researchers are now attempting to develop a microbe-derived version of artemisinin.

BANG – an acronym referring to a convergence of technologies whose operative units are Bits, Atoms, Neurons and Genes. The technologies are information technologies, nanotechnologies, cognitive neurosciences and biotechnology. BANG is referred to as NBIC (nano-bio-info-cogno) by the US government, CTEKS in Europe (Converging Technologies for the European Knowledge Society) and BioSystemics Synthesis in Canada.

Bioavailable – characteristic of a nutrient or pharmaceutical agent describing the degree to which the nutrient or medicine is useable by the body. Drugs formulated as nanoparticles seem to exhibit increased bioavailability.

Cytotoxic – toxic to cells. There are scientific data suggesting that some forms of nano-scale materials are cytotoxic.

Dendrimer – three-dimensional, nano-scale molecules so-named because the structures resemble trees with branches (*dendrons*). Dendrimers are able to host, either in the internal cavities or on the surface, smaller molecules that can be later released over time, making them promising drug delivery agents, as well as time-release delivery agents for perfumes and herbicides.

Disease Mongering – the marketing of sickness, which increases the numbers of people who self-identify or are identified as ill, in order to expand markets for those who sell pharmaceuticals or treatments.

Essential Medicines – According to the World Health Organization, essential drugs are those selected for their efficacy and safety to meet the priority health needs in a given country or region.

Global disease burden (GBD) – refers to a measurement of the total loss of health resulting from diseases and injuries, estimating mortality and morbidity by age, sex and/or region.

HyPE – an acronym referring to human performance enhancement technologies or drugs. Some HyPEs are developed with enhancement in mind; in other cases, the enhancement-potential is exploited after development.

Molecule – a collection of atoms held together by strong bonds. It usually refers to a particle with a number of atoms small enough to be counted (a few to a few thousand).

Microbicide – a pharmaceutical agent capable of killing viruses or pathogens.

Nanoparticle – a small piece of matter, composed of an individual element or a compound of elements, typically less than 100 nanometers in diameter. The term can refer to a wide range of materials, including the particulate matter expelled as car exhaust. Over the past two decades, engineered nanoparticles have been manufactured for commercial purposes, typically in order to take advantage of **quantum effects**.

Nanoshell – small particles, several hundred nanometers in diameter, manufactured using nano-engineering techniques, made up of a core material (usually silica) and a coating (usually gold)

Nanotube – cylinder-shaped molecule resembling rolled-up chicken wire. Nanotubes can be made of different substances, but most nanotube research focuses on tubes of pure carbon atoms. Carbon nanotubes are 100 times stronger than steel, impervious to temperatures up to 6,500 degrees Fahrenheit and only one to a few nanometers in width.

Orphan Disease – A disease that has not been "adopted" by the pharmaceutical industry because it provides little financial incentive to make and market new medications to treat or prevent it. Orphan diseases may be rare diseases that affect a small number of people or a common disease that has been neglected (e.g., tuberculosis, cholera, typhoid, and malaria) because it is far more prevalent in

the global South and in the North. (Adapted from: http://www.medterms.com/script/main/art.asp?articlekey=11418, viewed July 27, 2006)

Personalized Medicine – an approach to health-management that relies on a patient's genetic profile to reveal individual predispositions to particular diseases or levels of receptivity to particular pharmaceutical agents

Polymer – a substance, either natural or artificial, consisting of long-chain molecules. Plastic is the most well known artificial polymer.

Quantum Dot – is a nano-scale particle (a few hundred to a few thousand atoms) with extraordinary optical properties that can be customized by changing the size or composition of the particle. Quantum dots absorb light, then quickly re-emit the light in a different colour. Quantum dots can be "tuned" to any chosen wavelength simply by changing their size, useful for biological labeling in diagnostics and drug development.

Quantum Effects – optical, electrical or structural properties unique to the nano-scale, exhibited by nanomaterials smaller than around 100 nm. In general, only substances smaller than about 100 nm, in at least one dimension, exhibit quantum effects, though there are particular cases – such as polymers that have been reinforced with nanoparticles such that bonds have formed between the two materials – where special properties are exhibited even at sizes larger than 100 nm.

Synthetic Biology – refers to the construction of new living systems in the laboratory that can be programmed to perform specific tasks. When synthetic biology involves the integration of living and non-living parts at the nano-scale, it's synonymous with nanobiotechnology.

Targeted drug delivery – the ability to precisely direct a pharmaceutical agent to a desired location in the body, such as particular organs or specific cells.

Transhumanism – a position that sees humans in a relatively early phase of development and advocates the use of technologies to alter the current capabilities of human minds and bodies. Transhumanists embrace the notion of "better than well" people.

Notes

Notes for boxes and tables may be found at the end of the Notes section.

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4 David Rejeski, Director, Project on Emerging Nanotechnologies, Woodrow Wilson International Center for Scholars, Testimony before the US House of Representatives, Committee on Science, November 17, 2005.

5 *Ibid.*

6 European Science Foundation, *ESF Forward Look on Nanomedicine 2005*. On the Internet: http://www.esf.org/publication/214/Nanomedicine.pdf.

7 http://www.cihr-irsc.gc.ca/e/28268.html

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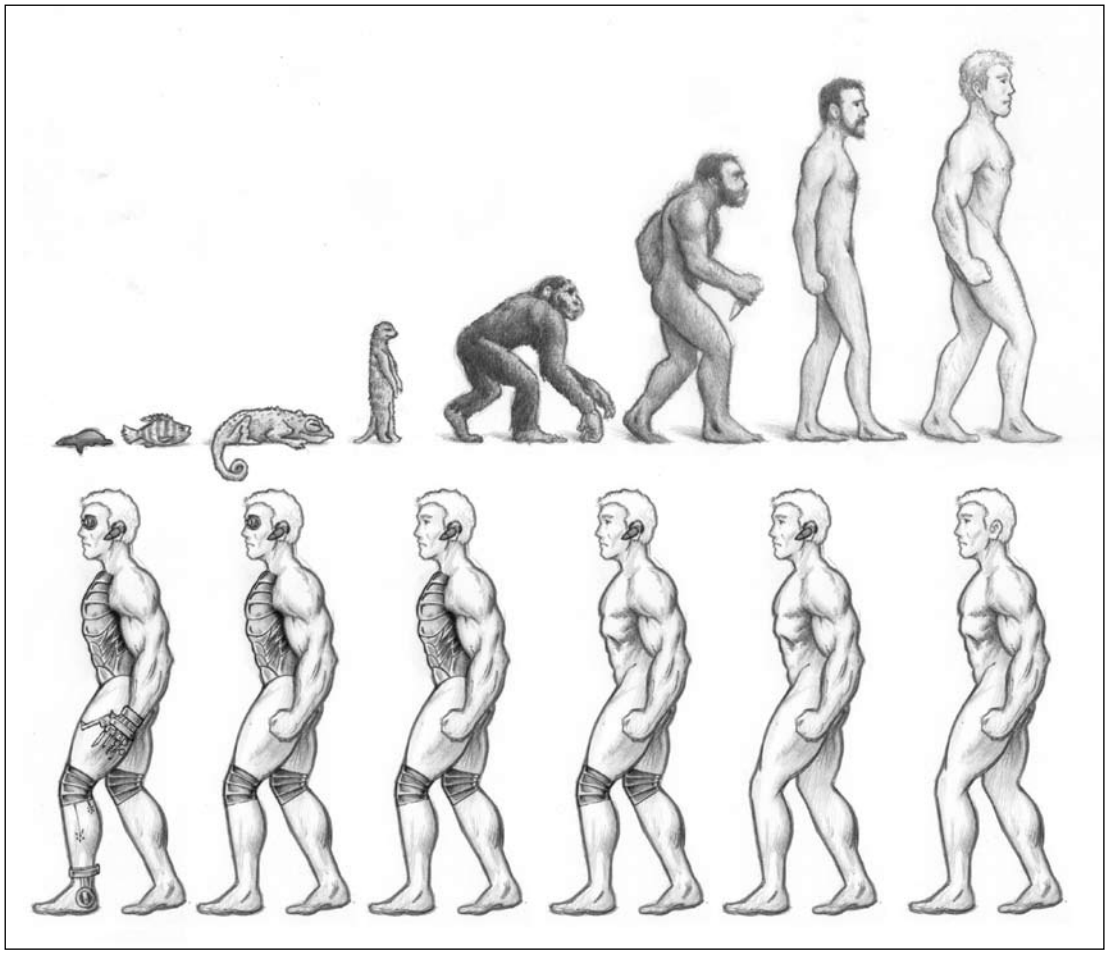
Notes for Table 4: Current Global Health Initiatives

1 Grand Challenges in Global Health Initiative was established in 2003 by the Gates Foundation and now includes the Wellcome Trust, the Canadian Institutes of Health Research and the Foundation for the National Institutes of Health (US) as partners. In June 2005, the Initiative granted 43 grants totaling $436.6 million to address 14 global health challenges. See: http//www.gcgh.org.

2 Financial information for Roll Back Malaria could not be found on the programme's web site, http://www.rbm.who.int/index.html. Approximate funding amounts are from Human Development Report Office, "Fund Profiles: Global Fund, GAVI, Fast Track Initiative, and Roll Back Malaria," Development Initiatives Occasional Paper 2005, p. 6.



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