Studies in Ethics, Law, and Technology

Volume 3, *Issue* 3 2009 *Article* 2

SMALL DIVIDES, BIG CHALLENGES? NANOTECHNOLOGIES AND HUMAN HEALTH

The Impact of Nanomedicine Development on North–South Equity and Equal Opportunities in Healthcare

Michael G. Tyshenko, *University of Ottawa*

Recommended Citation:
Tyshenko, Michael G. (2009) "The Impact of Nanomedicine Development on North–South Equity and Equal Opportunities in Healthcare," *Studies in Ethics, Law, and Technology*: Vol. 3: Iss. 3, Article 2.
DOI: 10.2202/1941-6008.1118

The Impact of Nanomedicine Development on North–South Equity and Equal Opportunities in Healthcare

Michael G. Tyshenko

Abstract

Nanomedicine applications are an extension of traditional pharmaceutical drug development that are targeting the most pressing health concerns through improvements to diagnostics, drug delivery systems, therapeutics, equipment, surgery and prosthetics. The benefits and risks to the individual have been extrapolated to include broader societal impacts of nanomedicine with concerns extending to inequitable distribution of benefits accruing to developed, or North countries, rather than developing, or South countries. Analysis reveals a great deal of overlap between the North and South's most serious health priorities which kill millions each year. A significant amount of nanomedicine research activity is also underway for the most pressing South country-specific health concerns. Nanomedicine development promises profound breakthroughs for both North and South countries; however, the existing inequities in pharmaceutical drug development, patenting, access and delivery remain significant barriers for South countries.

KEYWORDS: nanomedicine, equity, drug development, South countries, North countries

Introduction

Nanomedicine was defined by the National Institutes of Health as a new field that uses the application of nanotechnology for treatment, diagnosis, monitoring, and control of biological systems (Moghimi et al., 2005). Despite its relative infancy nanomedicine has generated a significant body of research as evidenced by peer review literature and a number of patents since 2003. Nanomedicine is predicted to be pervasive due to its convergence with other science disciplines including biology, genetics, biochemistry, chemistry, pharmacology and physics. Ongoing advances in research are validated and improved and some innovations are patented and commercialized. Previously, nanomedicine development has been measured by the output of nanomedicine-related research manuscripts and patents (Maclurcan, 2005; Wagner et al., 2006; Darshan and Tyshenko, 2010). Patents reflect the transfer of research to application and provide a good reflection of early sector nanomedicine development for various health priorities (Hullmann, 2006).

The nanotechnology North-South divide, including nanomedicine development, is believed to possess inequities similar to the digital and genomics divides that have occurred between industrialized and developing countries (Singer and Daar, 2001). Equity is characterized in terms of differing welfare standards of nation states or of groups of individuals. At the nation state level, equity can also be taken to mean an equitable sharing of natural resources such as water, land and air (Zhou, 2001). Equity is considered here as the equal opportunities for development and access to future nanomedicine applications for the North and South countries.

The divide is due to the gap between the science and the ethics of nanotechnology, and the differing vision of nanotechnology utility by developed (North) versus developing (South) countries (Mnyusiwalla et al., 2003). In order for nanotechnology to be developed in a socially responsible manner it was suggested that global equity is required (Roco, 2005). North countries have superior financial resources and more sophisticated negotiation skills for securing and developing nanomedicine application (Zhou, 2001). This can lead to North countries securing the most important, early nanomedicine patents and profits.

The North-South divide is the socio-economic and political division that exists between the wealthy developed countries, known collectively as "the North", and the poorer developing countries and the least developed countries collectively known as "the South." The countries are separated based on their level of development. The divide between North and South countries has significant impacts on global population health. Diseases in South countries hinder development. An example of this are investments into global health research with only 10% of the total funds being allotted to South countries that suffer 90% of the world's disease burden (Lown and Banerjee, 2006).

The North countries comprise the First World, with much of the Second World. North countries include: the Americas (Canada and the United States), Asian countries (Hong Kong, Macau,[1] Japan, Singapore, South Korea, Taiwan, Brunei, Malaysia and Thailand), Israel, Russia, European Union (EU) and European Free Trade Association countries,[2] and Oceania (Australia and New Zealand). Most developed countries share common health priorities such as obesity, diabetes, cardiovascular disease and other problems stemming from lifestyle and diet.

The South is described as having more pressing problems related to socio-economic conditions of its people compared to the North. The South is affected by high poverty levels, debt, disease and many South countries are limited for resources and access to the prerequisites necessary for development such as energy production, water treatment and sanitation. Without financial and technological resources South countries have difficulty attaining and maintaining development. The South comprises one-third of the world’s population, who reside mainly in rural areas (Zhou, 2001). The South includes all of Asia (except those countries previously excluded as North countries); Africa; the Middle East (except Bahrain, Qatar, Saudi Arabia and the United Arab Emirates); Central America and South America.

A common indicator of development and wealth is reflected by the Gross National Product (GNP) of a country. The GNP is calculated by dividing the total value of goods and services produced in the country by its population. It allows for comparison between countries levels of wealth. While GNP is the primary indicator for determining North-South divides other indicators include: Infant mortality rate (per 1000), life expectancy (years), daily calorie intake, adult literacy, percentage of GNP spent on education and agriculture, and percentage access to clean water. The United Nations defines South countries as Least Developed Countries (LDCs) which exhibit the lowest indicators of socio-economic development and possess the lowest Human Development Index.

The Organisation for Economic Co-operation and Development (OECD) further categorizes South countries into several groups based on the per capita Gross National Income (GNI) level. Categories include: Least Developed

[1] Hong Kong and Macau are Special Autonomous Regions of China.

[2] EU and European Free Trade Association countries include: Andorra, Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Monaco, Netherlands, Norway, Poland, Portugal, Romania, San Marino, Slovakia, Slovenia, Spain, Sweden, Switzerland, United Kingdom and the Vatican City.

DOI: 10.2202/1941-6008.1118

Countries (LDCs), Other Low-Income Developing Countries (Other LICs) (per capita GNI < $935 in 2007), Lower Middle-Income Developing Countries (LMICs) (per capita GNI $936-$3,705 in 2007), Upper Middle-Income Developing Countries (UMICs) (per capita GNI $3,706-$11,455 in 2007) (OECD, 2008). The GNI consists of the total value produced within a country (its gross domestic product and additional income received from other countries such as interest and dividends, less similar payments made to other countries).

Future Expectation and Framing of Nanomedicine's Benefits and Equity

Nanotechnology development has been framed with the idea that inequitable distribution of the benefits and profits will occur and accumulate to North countries and as a result the South countries will be exploited and have their development hindered (Salamanca-Buentello et al., 2005). The framing for nanomedicine, a recent offshoot of nanotechnology, is assumed to be the same with the development of nanomedicines that will result in an inequitable distribution of the benefits and profits that will accrue with North countries.

Nanotechnology development is framed as a North-South divide but comparing a list of the top ten causes of death for North and South countries shows that half are shared between the two. Both North and South countries have heart disease, lower respiratory infections, cerebrovascular disease, tuberculosis and chronic obstructive pulmonary disease in-common as their top, leading causes of death (Table 1). These five diseases which kill the largest numbers of individuals are being actively targeted by pharmaceutical companies regardless of whether individuals are from North or South countries. The remaining five leading causes of death for South countries (Rank #1: HIV/AIDS, #4 Diarrhoeal diseases, #6 Childhood diseases, #7 Malaria and #10 Measles) were examined to determine if nanotechnology development is also occurring and the results are summarized. The results of patent searches for "nano" and "cause of death" for South and North countries are shown in Table 2.

Table 1. The ten leading causes of mortality in the year 2001 for South and North countries reported by the WHO. Countries grouped by WHO Mortality Stratum, with South countries represented by those with "high" and "very high mortality". North countries represented by those with "low" and "very low mortality". The number of deaths in millions for each cause of death is given (UC Atlas, 2009).

Rank	South Countries Cause of Death	Number of Deaths (in millions)	Rank	North Countries Cause of Death	Number of Deaths (in millions)
1.	HIV/AIDS	2.68	1.	Ischaemic heart disease	3.51
2.	Lower respiratory infections	2.64	2.	Cerebrovascular disease	3.35
3.	Ischaemic heart disease	2.48	3.	Chronic obstructive pulmonary disease	1.83
4.	Diarrhoeal diseases	1.79	4.	Lower respiratory infections	1.18
5.	Cerebrovascular disease	1.38	5.	Trachea/bronchus/lung cancers	0.938
6.	Childhood diseases	1.22	6.	Road traffic accidents	0.669
7.	Malaria	1.10	7.	Stomach cancer	0.657
8.	Tuberculosis	1.02	8.	Hypertensive heart disease	0.635
9.	Chronic obstructive pulmonary disease	0.748	9.	Tuberculosis	0.571
10.	Measles	0.674	10.	Self-inflicted	0.499

DOI: 10.2202/1941-6008.1118

Table 2. Top ten leading causes of mortality in the year 2001 for South and North countries reported by the WHO from Table 1 (UC Atlas, 2009). Nanotechnology patents from the USPTO database (1976 to present) using keyword search strings, "nano" and "cause of death". USPTO patent full text database available at: http://patft.uspto.gov/netahtml/PTO/search-bool.html.

Rank	South Countries: Cause of Death	Keyword Search String	USPTO Patent Search	North Countries: Cause of Death	Keyword Search String	USPTO Patent Search
1.	HIV/AIDS	"nano and HIV"	1273	Ischaemic heart disease	"nano and ischaemic heart disease" "nano and heart disease"	3 205
2.	Lower respiratory infection	'nano and lower respiratory infection" "nano and lung infection"	1 3	Cerebrovascular disease	'nano and cerebrovascular disease"	14
3.	Ischaemic heart disease	"nano and ischaemic heart disease" "nano and heart disease"	3 205	Chronic obstructive pulmonary disease	"nano and chronic obstructive pulmonary disease"	79
4.	Diarrhoeal diseases	"nano and diarrhoea" "nano and diarrhea"	7 152	Lower respiratory infections	"nano and lower respiratory infections" "nano and lung infection"	1 3
5.	Cerebrovascular disease	"nano and cerebrovascular disease"	14	Trachea/bronchus/lung cancers	"nano and lung cancer"	639
6.	Childhood disease	"nano and childhood disease"	0	Road traffic accidents	N/A	-
7.	Malaria	"nano and malaria"	132	Stomach cancer	"nano and stomach cancer"	66
8.	Tuberculosis	"nano and tuberculosis"	232	Hypertensive heart disease	"nano and hypertensive heart disease" "nano and heart disease"	0 205
9.	Chronic obstructive pulmonary disease	"nano and chronic obstructive pulmonary disease"	79	Tuberculosis	"nano and tuberculosis"	232
10.	Measles	"nano and measles"	69	Self-inflicted	N/A	-

South-Specific Cause of Death #1: HIV/AIDS and Nanotechnology

In 2001 AIDS was the leading cause of death in non-industrialized regions (killing 2.68 million people, Table 1). In Sub-Saharan Africa it was estimated 1.9 million people succumbed to AIDS and it significantly impacts the population life expectancy of affected countries. The number of HIV/AIDS deaths is significantly less in North countries. In 2001, 169,000 people died of HIV/AIDS, or 5% of the world total for this disease (UC Atlas, 2009; Lopez et al., 2006) (Table 1). Global HIV prevalence has remained stable since early 2000-2001 with AIDS remaining one of the leading causes of death globally and the primary cause of death in Africa. The number of people living with HIV worldwide at the end of 2007 was estimated at 33.2 million (range: 30.6–36.1 million) (UNAIDS, 2008).

The use of synergistic combinations of three or more drugs against human immunodeficiency virus type 1 (HIV-1) known as Highly Active Antiretroviral Treatment (HAART) has markedly improved the clinical outcomes of HIV-1 infected individuals. Cell-mediated immunity can control viral replication and impede disease progression but HAART is unable to reconstitute HIV-specific host immunity as a way to eliminate the virus (Lori et al., 2007). Nanomedicine is being used to improve immunotherapy; for example, the chemically formulated nanoparticle used in the DermaVir Patch[3] has been developed to induce immune responses against HIV (Lori et al., 2005; 2007). Other applications, such as the Lateral flow *in vivo* diagnostic test for HIV using colloidal gold nanoparticles, are already available in the marketplace (Wagner et al., 2006). Patent database searches reveal a significant number of approved applications (1,273) dealing with nanotechnology and its application to HIV (Table 2).

South-Specific Cause of Death #4: Diarrheal Diseases and Nanotechnology

Several types of diarrhoeagenic *E. coli* strains have been identified worldwide, including enteropathogenic (EPEC), enterohaemorragic (EHEC), enteroinvasive (EIEC), enterotoxigenic (ETEC), Shiga toxin-secreting (STEC), diarrhoea-associated haemolytic (DHEC), entero-aggregative (EAAggEC), and cytolethal distending toxin-secreting (CDTEC) strains. The prevalence of these strains and the burden of disease they cause are unequal (Girard et al., 2006; WHO, 2009).

The annual global mortality from diarrhoeal diseases is estimated at about two million deaths per year (1.7 – 2.5 million deaths), ranking third among all

[3] DermaVir is a chemically formulated nanoparticle containing HIV-1 antigen-encoding plasmid DNA administered to support delivery of the nanoparticle to Epidermal Langerhans cells which transport the nanomedicine to draining lymph nodes.

DOI: 10.2202/1941-6008.1118

causes of infectious disease deaths worldwide (Kosek et al., 2003). ETEC strains remain a major cause of infantile diarrhoea in developing countries with the majority of deaths occur in children under five years of age (Black, 1993). STEC and Shigella infections accounts for 1.1 million deaths in developing countries, 60% of deaths occur in the under-five years of age (Niyogi, 2005). The WHO highlights the urgent need to develop a vaccine against ETEC and other enterohaemorragic *E. coli* strains (WHO, 2009).

In terms of morbidity, diarrhoeal diseases also impose a heavy burden on developing countries accounting for 1.5 billion instances of illness a year in children under five. The burden is highest in deprived areas where there is poor sanitation, inadequate hygiene and unsafe drinking water. In certain developing countries, epidemics of diarrhoeal diseases such as cholera and dysentery kill both children and adults. Other major diarrhoeal diseases include typhoid fever and rotavirus which is the main cause of severe dehydrating diarrhoea among children (WHO, 1999). Cellulose nanofibers are under development with potential for improving diagnostics and removal of pathogens (Bugusu, 2008). New nanotechnology applications pursuing water purification through development of inexpensive nano-filtration devices also has much potential to alleviate this burden of disease to South countries (Theron et al., 2008). The patent database keyword search revealed a number of patents (152) using nanotechnology to combat gastrointestinal pathogenic bacteria (Table 2).

South-Specific Cause of Death #6: Childhood Diseases and Nanotechnology

The WHO lists the leading causes of childhood mortality: malaria, Acute Respiratory Infection/pneumonia, diarrheal disease, malnutrition, birth complications and HIV/AIDS. Vaccine preventable childhood diseases include: poliomyelitis, diphtheria, pertussis, measles, tetanus, and *Haemophilus influenzae* type b. Malaria, diarrheal disease and HIV/AIDS are already listed in Table 1 as some of the leading categories of causes of death for South countries. South-specific causes of death for childhood diseases will focus on the significant cause of death attributed to Acute Respiratory Infections (ARIs). Pneumonia is the deadliest ARI and kills more children than any other childhood infectious disease. Most of these deaths (99%) related to ARIs occur in developing countries. In North countries childhood deaths from pneumonia are comparatively rare. ARIs and pneumonia affect children with low birth weight or those whose immune systems are weakened by malnutrition or other diseases revealing a synergistic, comorbid effect (WHO, 1999). Research has shown prevention of influenza pneumonitis infections by nano-sized conjugated dendritic polymers (Landers et al., 2002) and nano-emulsions (Myc et al., 2003; Donovan et al., 2000). No patents were found for this cause of death during the patent database keyword search likely due to patents that are directed towards specific pathogens (Table 2).

South-Specific Cause of Death #7: Malaria and Nanotechnology

The mortality rate in South countries from malaria increased throughout the 1990s affecting nearly one quarter of children in Sub-Saharan Africa (Lopez et al., 2006). More than a million deaths were reported from malaria in 2001 (Table 1). The high incidence of malaria imposes a huge economic burden on both families and governments through lost productivity, increased childhood mortality and high health care costs (WHO, 1999). Primaquine is one of the most widely used antimalarial and is the only currently available drug used against the relapsing form of malaria, especially cases caused by *Plasmodium vivax* and *Plasmodium ovale.* Experiments in a mouse model showed improved oral bioavailability, preferential liver uptake and effective antimalarial activity against *Plasmodium bergheii* infection when lipid nano-emulsion of primaquine was used (Singh and Vingkar, 2008). Patent database keyword search found 132 approved patents that dealt with nanotechnology and malaria (Table 2).

South-Specific Cause of Death #10: Measles and Nanotechnology

Measles is a highly contagious disease and results in high childhood mortality in South countries, estimated to account for hundreds of thousands of deaths annually. Measles primarily affects children and may result in more child deaths due to complications from pneumonia, diarrhoea and malnutrition (WHO, 1999). Recent nanotechnology research and patents are directed towards nanoparticles and nano-conjugates to improve drug delivery and vaccines (Andrianov and Payne, 1998; Andrianov et al., 1996; Kreuter, 1994; 1996). The patent database search revealed 69 patents; however, many of these patents were not specifically for measles nanomedicine applications. The lack of nanomedicine patents for measles is likely due to the fact that inexpensive, effective vaccines for measles are already available (Centers for Disease Control and Prevention, 2003).

Nanotechnology and North-South Intellectual Property

Early investors in nanotechnology (the US, Japan, and the EU) continue to aggressively pursue research and patents for nanomedicine innovations. These countries are already involved in developing policy and regulations for first generation (passive) nanoparticles. In contrast, developing countries are much less engaged in intellectual property development, regulation, determining how emerging technologies could affect their future, and often have weak institutional structures to control the application of such technology (Xue and Tisdell, 1999). The lack of foresight exercises for both nanotechnology and nanomedicine by developing countries is evident by the fact that there has been no systematic prioritization of applications of nanotechnology or nanomedicine targeted toward those challenges faced by the 5 billion people living in the developing world. A study of general nanotechnology patents by Compañó and Hullman (2002) from 1991-1999, showed nanotechnology patents are concentrated among the top country holders (92.1%). The only transitional or developing countries ranking in the top 15 holders were Israel and Russia.

Despite the lack of early investment some developing countries are now investing more in nanotechnology. China ranks third in the world behind the United States and Japan for the number of nanotechnology patents. Nanotechnology is expected to create approximately two million jobs worldwide by 2015. The majority of the jobs are predicted to be created in North countries including the US (0.8 million), Japan (0.5 million) with far fewer in South countries (0.2 million) in Asia Pacific (Hullman, 2006).

Nanotechnology patents are dominated by North countries. In a study of nanotechnology patents from 1976 to 2006 the top ten patents held by country were: United States, Japan, Germany, South Korea, France, Taiwan, Canada, Netherlands, United Kingdom and Switzerland as reported by the United States Patent and Trademark Office (USPTO). The potential of nanotechnology has been recognized in recent times by more countries as is seen with increasing numbers of patents held by Asian countries (Roco, 2005). South Korea and Taiwan have published 209 patents and 161 patents, respectively, since 2000 moving into the top ten countries for this period (Chen et al., 2008).

Roco (2005) estimated the government nanotechnology R&D expenditures from 1997–2004 revealing South countries have increased investments since the year 2001. Nantoechnology is not exclusively for the benefit of developed countries like the US, EU and Japan. Other countries with smaller investment funds are continuing to research and receive patents in nanotechnology and nanomedicine. Even though investments are smaller South countries are targeting nanomedicine research and applications to tackle problems of higher regional priority (Court et al., 2004; Salamanca-Buentello et al., 2005). Inequity in patents and research investments between North and South countries is clearly evident. Moreover, generating patents by South countries does not guarantee access to new nanomedicines.

Nanomedicine and Health-Related Intellectual Property for North and South Countries

Nanomedicine as a formal research area is about a decade old with the first peer review papers citing the term in the year 1999 (Darshan and Tyshenko, 2010). There has been an exponential growth of research in "nanomedicine" and "nanotechnology and medicine" as indicated by the increasing number of peer review research publications since 2001. Despite its relative infancy nanomedicine has generated a significant body of research as evidenced by peer review literature and a number of patents since 2003 (Darshan and Tyshenko, 2010).

Maclurcan (2005) assessed health-related medical nanotechnology patents using keyword searches of all available patent databases finding 1,256 patents shared by 35 countries; the three leading countries were the US (32.8%), China (20.3%) and Germany (12.9%). China is considered a South country but ranks second for medical nanotechnology patents. While the majority of patents (88%) were held by just seven countries the study found that health-related nanotechnology patents were held by a number of South, transitional countries including South Korea (3.9%), Israel (0.9%), Russia (0.5%), Taiwan (0.3%), the British Virgin Islands (0.2%), Hong Kong (0.2%), Hungary (0.2%), Poland (0.2%), Singapore (0.2%), Bermuda (0.1%) and Slovenia (0.1%). Also, developing country patent holders included China (20.3%), India (0.5%), Brazil (0.1%), and Serbia and Montenegro (0.1%). The greater number of nanomedicine patents held by South countries reflects the increased interest and research by these countries after the year 2000 and coincides with nanomedicine as an emerging area of research which also occurred around this time (Darshan and Tyshenko, 2010).

Court et al. (2004) showed a surprising level of nanotechnology research and development (R&D) occurring in South countries. Several developing countries have launched nanotechnology initiatives as a way to increase their capacity and economic growth (Court et al., 2004). Salamanca-Buentello et al. (2005) detail several significant investments by South countries in nanotechnology including India, Brazil, China, South Africa, Thailand, the Philippines, Chile, Argentina, and Mexico. The involvement of South countries and investments into nanotechnology and nanomedicine have increased dramatically in the last decade. By 2005, Maclurcan (2005) showed 62 South countries had engaged nanotechnology on a national level with investments. A further 16 South countries showed individual and group research in nanotechnology. At this time another 14 countries expressed interest in engaging in and funding small amounts for nanotechnology research. However, for many of the less-developed countries, the current barriers present themselves at the earliest stages of R&D entry (Maclurcan, 2005).

North–South partnerships have occurred which may help minimize the nanotechnology divide. For example, US funding of nanotechnology research in South-east Asia and EU funding with third partner countries (Argentina, Chile, China, India and South Africa) focuses on technological co-operation which includes nanotechnology development (Court et al., 2003).

Hassan (2005) argues that heavy investments by early investors will not lead to a North-South nanodivide comparable to the divide that has characterized biotechnology and global information technologies. The reasoning provided by Hassan (2005) relies heavily on the nanotechnology development of China, which is used as the example of a South country. China began investments and infrastructure for nanotechnology much earlier than other South countries. Beginning in 1986, China made significant investments into its National High-Tech Research and Development Program (863 Program) to increase China's high-tech industry, research and development, socio-economic development and national security. The Chinese Academy of Sciences has been a center for nanotechnology in the country and created the largest research institution network in the world, the CAS Nanotechnology Engineering Center Co., Ltd (CASNEC). The institution works with large manufacturers to help the integration of nanotechnology with existing industries and develop competitive nanotechnology products. In addition, China is highly atypical for its size, human capital for nanotechnology with a high number of science and engineering PhDs and its exceptional economic growth (Burnett and Tyshenko, 2010). The conclusion that a North-South divide will not occur for nanotechnology is likely incorrect since China, as a South country, is not representative of other South countries for economic growth and nanotechnology development.

Conclusions

Both North and South countries share many of the same causes of death (Table 1). Analysis shows a significant amount of nanotechnology and nanomedicine development is occurring for South-specific causes of death (Table 2) for some diseases (HIV, pathogenic bacteria and malaria) but not for all (childhood diseases and measles). Previous medical research has produced solutions to most of the serious health problems affecting developing South countries. For example, there is international recognition of the high burden of disease associated with measles that causes extensive childhood mortality in South countries. Despite this knowledge and the existence of a safe, effective, and inexpensive vaccine for measles it remains the leading cause of vaccine-preventable childhood mortality (Centers for Disease Control and Prevention, 2003). Moreover, other diseases such as mumps, rubella, diphtheria, tetanus, pertussis, *Haemophilus influenzae* type b (Hib) disease, polio and yellow fever can be controlled by vaccination (Peek et al., 2008).

Nanomedicine is an extension of the existing drug discovery and patent system with companies that secure patents to recoup research and development investments. Many applications have arisen due to the convergence of nanotechnology's application to medicine. The concern for nanomedicine is that development and access will be similar to the many promises of past technological revolutions that were challenged by the inequities of global development and domestic technology distribution. The distribution of nanotechnology innovations is skewed towards North countries but South countries are investing in and acquiring patents for nanomedicine. Future nanomedicine may empower local healthcare auxiliaries, in rural settings worldwide, to address diagnostic and therapeutic concerns by reducing reliance on trained specialists or technical assistance. For example, lab on chip diagnostics using nanotechnology and 'omics' research may greatly simplify diagnosis through blood or body fluid screening and allow for improved healthcare in remote areas. The discussion presented here focused on patents as an indicator of South country nanomedicine development; however, as a caveat patents by themselves accrued to South countries may not translate into readily available nanomedicines.

The South vision of new nanomedicine to combat regionally specific causes of death is not shared entirely by pharmaceutical companies based in North countries. In addition, part of the problem lies in the initial North-South framing which focuses on the activity of countries. It overlooks the presence and potential activities of multinational corporations and pharmaceutical companies in the development process and technology transfer activities. In order to meet the goals of equity and sustainable development, both the North and the South should have a clear understanding, from a geographic, cultural, social-structural and intergenerational perspective, of their rights and responsibilities for nanomedicine development.

The causes of South country inequality for nanomedicine can be linked to three main reasons. The first is the current development of nanotechnology for nanomedicine with research into novel improvements in drug targeting, drug design and therapeutics result in patents. The current patenting system benefits more developed North countries as they have greater capital for research. Early patents can create 20 year monopolies excluding others during a critical time window of innovation. The same South access problems that existed for pharmaceutical drug development and delivery by multinational pharmaceutical companies (North countries) versus needs of the South countries will not be changed by ongoing nanomedicine development. Applications will be developed

DOI: 10.2202/1941-6008.1118

for profit and the huge costs of investment results in high drug prices and support of the patent system to recoup R&D costs. Patents are concentrated by North countries but the numerous patents and development by South countries lessen North-South divide arguments. Regionally specific infectious diseases are being targeted by individual countries with smaller research funding. New nanomedicine applications have the potential to empower a local response to challenges such as the diagnosis and treatment of infectious disease.

Secondly, for nanotechnology the fractured nature of South countries with differing regional needs suggests that different approaches and combinations of activities will be needed. Collectively, unlike North countries which are more homogeneous, South countries have disparate GNI levels combined with other indicators. For example, one South country may have a higher GNI but possess less access to clean water than another South country with a lower GNI but more natural resources, clean water and higher daily caloric intake. Even though countries have been designated as North or South, several newly industrialized or rapidly developing countries such as South Korea, Taiwan, Argentina, Mexico, Brazil, Peru, and Chile now have more in common with the industrialized North than with other South countries. The result is health priorities now vary greatly between South countries with distinctly different regional concerns. Clearly the future vision for nanotechnology development differs not only between the North and South but also between South countries.

Thirdly, equipment needed to pursue nanotechnology research is very expensive (Patil, 2005). In South countries with the lowest GNIs there is often a lack of funds for purchasing basic equipment needed for nanotechnology research such as Atomic Force Microscopes and maintaining nanoparticle containment laboratories. The Atomic Force Microscope, which is an essential nanotechnology research tool can cost as much as approximately $1.5 million USD. The monetary infrastructure investments needed to conduct competitive research may not be feasible for LDCs, Other LICs and LMICs. The expensive nature of nanotechnology research will tend to concentrate commercialization of nanotechnology to LMIC and UMIC South countries and large corporations in affluent North countries (Tyshenko, 2010). Worldwide funding for nanotechnology development differs based on the sheer amount of capital available for research and development investment resulting in a stratification of wealthy versus poor countries but also of South countries.

Thus, the central issue for future South nanomedicine development is how to develop the most effective strategies to decrease existing inequities ensuring access to new nanomedicines. One workable solution is focusing on partnering and increasing partnerships for South countries. For example, initiatives such as the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), the Gates Foundation, the Clinton Foundation and other organizations partnering with South countries can help to stimulate research, provide needed programs, increase access to medicines and improve knowledge transfer in LMIC and UMIC countries. Such partnering provides an excellent model to use for future nanomedicine access.

In 2003, PEPFAR was launched to combat global HIV/AIDS providing funds to develop prevention, treatment and care programs for 120 countries. PEPFAR specifically targets a subset of 12 focus countries with the lowest per capita incomes to provide additional support (Committee for the Evaluation of the President's Emergency Plan for AIDS Relief, PEPFAR, Implementation, 2007). In the future, similar types of initiative for nanomedicine access programs could be developed by such initiatives targeted to help the lowest GNI countries.

Other organizations, such as the Gates foundation, have provided funds for developing vaccines and programs through partnerships to eradicate malaria and combat tuberculosis in South countries (Bill and Melinda Gates Foundation, 2007; 2009). In 2004, the William J. Clinton Presidential Foundation; the Global Fund to Fight AIDS, Tuberculosis and Malaria; the World Bank; and Unicef joined forces to help more than 100 countries that receive aid from the World Bank, Global Fund and UNICEF to get inexpensive generic AIDS drugs and discounted AIDS tests (Henry Kaiser Family Foundation, 2009). In a similar initiative the Clinton Foundation in 2009 announced agreements with two drug companies to reduce the cost of second-line antiretrovirals (ARVs) and a key tuberculosis drug for low and middle income countries (Plus News, 2009).

Future nanomedicine access and programs for LDCs, other LICs, LMICs and UMIC countries could be based on such initiatives. Multi-country and multi-organization partnership efforts clearly have a role in the future helping South countries to improve healthcare programs, gain access to nanomedicines and to develop suitable delivery programs.

Some targeted South country nanotechnology development and North-South partnerships have been initiated but much more work remains to reduce the North-South divide for nanomedicines. Decreasing inequity gaps will require significantly greater commitment by the North countries, organizations, and individuals who have the ability to increase technology transfer and partnerships (Staton and Harding, 2004). Salamanca-Buentello et al. (2005) remind us that nanotechnology has the potential to generate enormous health benefits for the more than 5 billion people living in the developing world from such applications outside of nanomedicine including new water purification technologies. Partnering should include these nano-developments as well along with nanomedicine for a more integrated healthcare approach. South access to nanomedicine for specific regional concerns, pursuing partnerships (North-South and South-South) and future nano-water purification technologies will provide

DOI: 10.2202/1941-6008.1118

additional benefits for improving population health beyond what pharmaceutical companies and North countries will provide.

References

Andrianov A.K. and Payne L.G. 1998. Polymeric carriers for oral uptake of microparticulates. Adv Drug Deliv Rev. 34(2-3): 155-170.

Andrianov A.K., Jenkins S.A., Payne L.G. and Roberts B.E. 1996. Hydrogel microencapsulated vaccines, US Patent Number 5,529,777. Available: http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&p=1&u=%2Fnetahtml%2FPTO%2Fsearch-bool.html&r=9&f=G&l=50&co1=AND&d=PTXT&s1=Andrianov&s2=nano&OS=Andrianov+AND+nano&RS=Andrianov+AND+nano.

Bill and Melinda Gates Foundation. 2007. Bill and Melinda Gates Call for New Global Commitment to Chart a Course for Malaria Eradication. October 17. Available: http://www.gatesfoundation.org/press-releases/Pages/course-for-malaria-eradication-071017-2.aspx.

Bill and Melinda Gates Foundation. 2009. Chinese Government and Foundation Announce Partnership to Fight Tuberculosis. April 1. Available: http://www.gatesfoundation.org/press-releases/Pages/partnering-with-chinese-government-to-stop-tb-090331.aspx.

Black R.E. 1993. Epidemiology of diarrhoeal disease: implications for control by vaccines. Vaccine. 11(2):100-6.

Bugusu B. 2008. Improving food through nanoscience. Food Technology. September: 34-39. Available: http://members.ift.org/NR/rdonlyres/D8FF91A0-201B-4E45-85F0-34DAA5FECB4D/0/0908feat_nano.pdf.

Burnett K. and Tyshenko M.G. 2010. A comparison of human capital levels and the future prospect of the nanotechnology industry in early sector investors and recent emerging markets. International Journal of Nanotechnology. 7(2-3):187-208.

Centers for Disease Control and Prevention. 2003. Update: global measles control and mortality reduction-worldwide, 1991-2001. MMWR Morb Mortal Wkly Rep. May 23. 52(20): 471-5.

Chen H., Roco M.C., Li X. and Lin Y. 2008. Trends in nanotechnology patents. Nature Nanotechnology 3, 123 – 125.

Compañó R. and Hullman A. 2002. Forecasting the development of nanotechnology with the help of science and technology indicators, Nanotechnology, 13: 243-47.

Committee for the Evaluation of the President's Emergency Plan for AIDS Relief (PEPFAR) Implementation, 2007. PEPFAR Implementation: Progress and Promise. J. Sepulveda, C. Carpenter, J. Curran, W. Holzemer, H. Smits, K. Scott, and M. Orza, Editors. National Academies Press, Washington. D.C. United States. pp. 400.

Court E, Daar AS, Martin E, Acharya T, Singer PA (2004) Will Prince Charles et al diminish the opportunities of developing countries in nanotechnology? Available: http://nanotechweb.org/cws/article/indepth/18909 .

Darshan S. and Tyshenko M.G. 2010. Identifying recent trends in nanomedicine development. International Journal of Nanotechnology. 7(2-3): 173-186

Donovan B.W., Reuter J.D., Cao Z., Myc A., Johnson K.J. and Baker JR Jr. 2000. Prevention of murine influenza A virus pneumonitis by surfactant nano-emulsions. Antivir Chem Chemother. 11(1):41-9.

Girard M.P., Steele D., Chaignat C.L. and Kieny M.P. 2006. A review of vaccine research and development: human enteric infections. Vaccine. 24(15): 2732-50.

Hassan MH. 2005. Nanotechnology. Small things and big changes in the developing world. Science. 309(5731): 65-6.

Henry Kaiser Family Foundation. 2009. Clinton Foundation, Global Fund, World Bank, UNICEF Extend Low-Cost Generic AIDS Drug Prices to More Than 100 Countries, April 06, 2004. Available: http://www.kaisernetwork.org/daily_reports/rep_index.cfm?hint=1&DR_ID=23059.

Hullmann A. 2006. The economic development of nanotechnology – an indicators based analysis, European Commission, DG Research, Unit "Nano S&T – Convergent Science and Technologies". Available: http://cordis.europa.eu/nanotechnology.

Kosek M, Bern C, Guerrant RL. 2003. The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000. Bull World Health Organ. 81(3): 197-204.

Kreuter J. 1994. Drug targeting with nanoparticles. Eur J Drug Metab Pharmacokinet. 19(3): 253-6.

Kreuter J. 1996. Nanoparticles and microparticles for drug and vaccine delivery. J Anat. 189(3): 503-5.

Landers J.J., Cao Z., Lee I., Piehler L.T., Myc P.P., Myc A., Hamouda T., Galecki A.T., Baker J.R. Jr. 2002. Prevention of influenza pneumonitis by sialic Acid-conjugated dendritic polymers. J Infect Dis. 186(9): 1222-30.

Lopez A.D., Mathers C.D., Ezzati M., Jamison D.T. and Murray C.J. 2006. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. Lancet. 367(9524): 1747-57.

Lori F., Trocio J., Bakare N., Kelly L.M. and Lisziewicz, J. 2005. DermaVir, a novel HIV immunisation technology. Vaccine. 23(17-18): 2030-4.

Lori F., Calarota S.A. and Lisziewicz J. 2007. Nanochemistry-based immunotherapy for HIV-1. Curr Med Chem. 14(18): 1911-9.

Lown B. and Banerjee A. 2006. The developing world in The New England Journal of Medicine. Globalization and Health. 2(3): 1-5.

Maclurcan D.C. 2005. Nanotechnology and developing countries part 2: what realities? International Journal of Nanotechnology Online. October. 1: 1-19. Available: http://www.azonano.com/Details.asp?ArticleID=1429

Moghimi S.M., Hunter A.C. and Murray J.C. 2005. Nanomedicine: current status and future prospects, FASEB Journal. 19(3): 311-330.

Mnyusiwalla A., Daar A.S. and Singer P.A. 2003. Mind the gap: science and ethics in nanotechnology. *Nanotechnology.* 14: R9-13.

Murray C.J.L., Lopez A.D., Mathers C.D. and Stein C. 2001. The global burden of disease 2000 project: aims, methods and data sources. Research Paper No. 01 .1. Burden of Disease Unit, Harvard University, Cambridge. USA. Available: http://www.hsph.harvard.edu/burdenofdisease/publications/papers/gbd2000.pdf.

Myc A., Kukowska-Latallo J.F., Bielinska A.U., Cao P., Myc P.P., Janczak K., Sturm T.R., Grabinski M.S., Landers J.J., Young K.S., Chang J., Hamouda T., Olszewski M.A., Baker J.R. Jr. 2003. Development of immune response that protects mice from viral pneumonitis after a single intranasal immunization with influenza A virus and nanoemulsion. Vaccine. 21(25-26): 3801-14.

Niyogi SK. 2005. Shigellosis. J. Microbiol. 43(2):133-43.

OECD. 2008. DAC list of ODA recipients, effective for reporting on 2008, 2009 and 2010 flows. Paris, France. Available:
http://www.oecd.org/dataoecd/62/48/41655745.pdf.

Patil R. 2005. If tomorrow comes. Available:
http://www.indianexpress.com/full_story.php?content_id=62323.

Peek L.J., Middaugh C.R. and Berkland C. 2008. Nanotechnology in vaccine delivery. Adv Drug Deliv Rev. 60(8): 915-28.

Plus News. 2009. Clinton Foundation closes deal to slash cost of second-line ARVs. September 30. Available:
http://www.plusnews.org/Report.aspx?ReportId=85623.

Roco M.C. 2005. International perspective on government nanotechnology funding in 2005. Journal of Nanoparticle Research. 7: 707–712.

Salamanca-Buentello F, Persad DL, Court EB, Martin DK, Daar AS, Singer PA. 2005. Nanotechnology and the developing world. PLoS Med. 2(5):e97.

Singer P.A. and Daar A.S. 2001. Harnessing genomics and biotechnology to improve global health equity. Science 294: 87-9.

Singh K.K. and Vingkar S.K. 2008. Formulation, antimalarial activity and biodistribution of oral lipid nanoemulsion of primaquine. Int J Pharm. 347(1-2): 136-43.

DOI: 10.2202/1941-6008.1118

Staton D.M. and Harding M.H. 2004. Protecting child health worldwide. Implementation is the biggest challenge slowing efforts to reduce childhood morbidity and mortality in developing countries. Pediatr Ann. 33(10): 647-55.

Theron J., Walker J.A. and Cloete T.E. 2008. Nanotechnology and water treatment: applications and emerging opportunities. Crit Rev Microbiol. 34(1): 43-69.

Tyshenko M.G. 2010. Nanotechnology innovation as a deus ex machina and potential effects on sustainability in a global context. International Journal of Nanotechnology. 7(2-3): 209-223.

UC Atlas. 2009. UC atlas of global inequity. Cause of death. Available: http://ucatlas.ucsc.edu/cause.php.

UNAIDS. 2008. 07 UNAIDS annual report. Geneva, Switzerland. pp. 51. Available:http://data.unaids.org/pub/Report/2008/jc1535_annual_report07_en.pdf

Wagner V., Dullaart A., Bock A.K. and Zweck A. 2006. The emerging nanomedicine landscape. Nat Biotechnol. 24(10): 1211-7.

WHO. 1999. Chapter 2. Six diseases cause 90% of infectious disease deaths *in* Removing Obstacles to Healthy Development. Geneva, Switzerland. Pp. 68. Available:
http://www2.alliance-hpsr.org/infectious-disease-report/pages/ch2text.html.

WHO. 2009. Initiative for vaccine research (IVR). Available: http://www.who.int/vaccine_research/diseases/diarrhoeal/en/index4.html

Xue D. and Tisdell C. 1999. Safety and socio-economic issues raised by modern biotechnology. Working paper No. 36. Economics, Ecology and Environment Working Papers from University of Queensland, School of Economics, Queensland, Australia. Available:
http://ageconsearch.umn.edu/bitstream/47995/2/WP36.pdf

Zhou P. 2001. North-South dialogue. Tiempo - Issue 40/41, September 2001. Available online:
http://www.tiempocyberclimate.org/portal/archive/issue4041/t4041a1.htm.