

Health Innovation in Developing Countries to Address Diseases of the Poor

Carlos Morel¹, Denis Broun², Ajit Dangi³, Christopher Elias⁴, Charles Gardner⁵, RK Gupta⁶, Jane Haycock⁷, Tony Heher⁸, Peter Hotez⁹, Hannah Kettler¹⁰, Gerald Keusch¹¹, Anatole Krattiger¹², Fernando Kreutz¹³, Keun Lee¹⁴, Richard Mahoney¹⁵, R.A. Mashelkar¹⁶, Hong-ki Min¹⁷, Stephen Matlin¹⁸, Mandi Mzimba¹⁹, Joachim Oehler²⁰, Robert Ridley²¹, Pramilla Senanayake²², Halla Thorsteinsdóttir²³, Peter A. Singer²⁴, Mikyung Yun²⁵

The concepts presented here were crystallized at a meeting convened by the Rockefeller Foundation at the Bellagio Study and Conference Center, 10–13 May 2004. Twenty-three participants attended from Brazil, Canada, France, India, Korea, South Africa, the United Kingdom and the USA. Following the meeting, a number of other individuals made significant intellectual contributions, and they are included as authors of this paper. The authors are grateful to all who contributed to this paper and to the Rockefeller Foundation for financial support. The views expressed are nevertheless those of the authors in their individual capacities and do not necessarily reflect those of their respective institutions, nor of the publishers, editors and supporters of *Innovation Strategy Today*.

¹ *Scientific Coordinator*, Center for Technological Development in Health, Oswaldo Cruz Foundation (FIOCRUZ), Rio de Janeiro, Brazil

² *Programme Manager*, Management Sciences for Health, Ferney-Voltaire, France

³ *President*, Organization of Pharmaceutical Producers of India, Bombay, India

⁴ *President*, Program for Appropriate Technology in Health, Seattle, USA

⁵ *Associate Director*, Health Equity, The Rockefeller Foundation, New York, USA

⁶ *Head*, Intellectual Property Management Division, Council for Scientific and Industrial Research, New Delhi, India

⁷ *First Secretary*, Mission of the United Kingdom to the United Nations, United Kingdom

⁸ *Director*, UCT Innovation, University of Cape Town, Cape Town, South Africa

⁹ *Professor*, George Washington University, Washington, D.C., USA

¹⁰ *Program Officer*, Global Health Programs, The Bill and Melinda Gates Foundation, Seattle, USA

¹¹ *Provost and Dean For Global Health*, Boston University School of Public Health, Boston, USA

¹² *Research Professor*, Arizona State University, Tempe, USA and Adjunct Professor, Cornell University, Ithaca, USA

¹³ *CEO*, FK Biotechnology, Brazil

¹⁴ *Professor*, Department of Economics, Seoul National University, Seoul, Korea

¹⁵ **Corresponding Author**. *Research Professor*, Arizona State University, Tempe, USA. Phone +1-928-282 1608
richard.mahoney@asu.edu

¹⁶ *Director General*, Council for Scientific and Industrial Research, New Delhi, India.

¹⁷ *Director*, Biological Products Division, Korean Food and Drug Administration, Seoul, Korea

¹⁸ *Executive Director*, Global Forum for Health Research, Geneva, Switzerland

¹⁹ *Science Attaché*, South African Embassy, Brussels, Belgium

²⁰ *General Manager*, The Concept Foundation, Bangkok, Thailand

²¹ *Director*, Special Programme for Research and Training in Tropical Diseases (TDR), World Health Organization (WHO), Geneva, Switzerland

²² *Chair*, Global Forum for Health Research, Geneva, Switzerland

²³ *Assistant Professor*, Canadian Program on Genomics and Global health, University of Toronto Joint Centre for Bioethics and Departments of Public Health Sciences, Toronto, Canada.

²⁴ *Sun Life Financial Chair and Director*, University of Toronto Joint Centre for Bioethics, and Professor of Medicine, University of Toronto and University Health Network, Toronto, Canada

²⁵ *Research Fellow*, Korea Institute for International Economic Policy, Seoul, Korea

Morel C, D Broun, A Dangi, C Elias, C Gardner, RK Gupta, J Haycock, T Heher, P Hotez, H Kettler, G Keusch, A Krattiger, F Kreutz, K Lee, R Mahoney, RA Mashelkar, Hong-ki Min, S Matlin, M Mzimba, J Oehler, R Ridley, P Senanayake, H Thorsteinsdóttir, PA Singer and Mikyung Yun. 2005. Health Innovation in Developing Countries to Address Diseases of the Poor. *Innovation Strategy Today* 1(1):1-15. www.biodevelopments.org/innovation/index.htm

Abstract

There is a great unmet need for health technologies to address diseases of the poor in developing countries. At the same time, there is a rapidly growing capability to undertake health innovation^a in many developing countries (Innovative Developing Countries - IDCs). IDCs have the capacity to develop, manufacture, ensure safety, and market new health products and to develop, test and introduce new health policies or strategies. They are distinguished by their rapidly growing strength in health innovation as illustrated by increasing patenting and publishing activities; increasing investments in technology by both the public and private sectors; rapidly growing number of health technology companies^b; and health systems able to analyze, evaluate and adopt new practices and technologies.

This innovation capability provides an underleveraged opportunity to accelerate the development of new products, policies and strategies for diseases of the poor. We call for the formation of an *Initiative for Health Product Innovation in Developing Countries*. Its primary mission will be to accelerate the translation

of new knowledge into health innovations relevant to the diseases of the poor and to economic growth, taking into account national priorities and sensitivities. The Initiative could promote innovation through programs to (i) support research on health innovation systems; (ii) promote collaboration and coordination among countries to develop, disseminate and implement good practices; and (iii) implement demonstration projects.

Such an Initiative would help maximize existing and growing investments by developing countries in health research, and complement global efforts to address health disparities and achieve the Millennium Development Goals.¹

^a We use the term 'health innovation' to include the development of new drugs, vaccines and diagnostics as well as new techniques in process engineering/manufacturing and new approaches/policies in health systems and services.

^b Throughout this paper, we will refer to specific developing countries. These are illustrative and there are many additional countries with strengths in innovation.

Southern Needs, Northern Response and Global Strategies

Recent evidence shows that improved health is more than a consequence of development. It is a central input into economic and social development and poverty reduction. Good health, economic development and individual economic well being are intimately interdependent. The importance of investing in health cannot be overstated.² The magnitude of the health problems facing the poor in developing countries are immense.^{3,4} Approximately 10 million children die each year with "under-nutrition as an underlying cause of child deaths associated with infectious diseases, the effects of multiple concurrent illnesses, and recognition that pneumonia and diarrhea remain the diseases that are most often associated with child deaths."⁵ In addition, global health experts are increasingly recognizing the growing relative importance of chronic diseases in the developing world where, in contrast to the infectious diseases that primarily affect children, middle aged and older people are the most vulnerable. Chronic diseases are the world's largest cause of death with 33 million deaths worldwide in

2003. The leading chronic diseases are cardiovascular disease, cancer, chronic respiratory disease, and diabetes.⁶

There are many interventions and strategies for improving health including strengthening health systems to improve the delivery of goods and services, education about desirable individual behavior, and introduction of water and sanitation systems. However, limitations of existing technologies, or the absence of appropriate technologies and other innovations, impede the achievement of desired health improvement goals. All health interventions draw upon innovations as essential tools to achieve the desired health improvement outcome. Such innovations include vaccines to prevent HIV, malaria, respiratory, and diarrhoeal diseases; drugs to treat TB, malaria, cancers, and diabetes; other hardware such as weighing scales; software such as disease surveillance systems; and diagnostics and medical devices. These are a necessary part of a broader package of interventions including improvements in health delivery, surveil-



lance, and policy formulation to improve the health of those most in need in the developing world.

Efforts to accelerate the development and distribution of health products for diseases of the poor have intensified over the past decade. Product development public private partnerships (PD-PPPs) have been established to develop new vaccines and drugs against HIV, malaria, TB, diarrhea and other infectious diseases, and related diagnostics and medical devices. These partnerships include the International AIDS Vaccine Initiative (IAVI), the International Partnership for Microbicides (IPM), the Medicines for Malaria Venture (MMV), the Malaria Vaccine Initiative (MVI), the Global Alliance for TB Drug Development (TB Alliance), the Aeras Global TB Vaccine Foundation, the Human Hookworm Vaccine Initiative (HHVI), the Foundation for Innovative New Diagnostics (FIND), the Drugs for Neglected Diseases Initiative (DNDi) and the Institute for OneWorld Health. These initiatives have made significant pro-

gress, but are still relatively young and have therefore not yet achieved their intended goals.⁷

In addition to the PD PPPs, major global funds have been also established over the past five years to procure and distribute existing drugs and vaccines. These include the Vaccine Fund that works with the Global Alliance for Vaccines and Immunizations (GAVI) and the Global Fund to Fight AIDS, Tuberculosis and Malaria. Sustained and increasing support from donors will be needed for product development and procurement efforts to have their desired impact over the next decade. Access by the poor, either to existing or new products, depends upon numerous factors, but especially health delivery systems. The need for more attention, research and resources in this area was the subject of the annual meeting of the Global Forum for Health Research, and the World Health Organisation (WHO)-Mexico Ministerial Summit on Health Research, both held in Mexico City November 16-20, 2004⁸.

Growing Capabilities of Developing Countries in Health Innovation

One commonly identified impediment to effective health systems in developing countries is the difficulty of translating promising product concepts into affordable and accessible products. However, at least in some developing countries, this difficulty is beginning to be addressed. The rapidly growing health innovation capabilities of some developing countries represent a phenomenon that should complement the PD PPP efforts described above.

The concept of “health innovation systems” encompasses interlinked components including education, R&D, manufacture, domestic and export markets, intellectual property (IP) management, regulatory systems and the national policies that affect all of these (including public-private partnerships)⁹ ¹⁰. An effective health innovation system, extending from concept research through delivery at the program and health systems level, depends upon the design and implementation of policies that recognize the dynamic linkages among all components of the system.

Developing countries themselves are building innovative capacity for new health technologies, products and services¹¹. Collectively they already invest at least \$2.5 billion per year in health research.¹² This compares with about \$200 million per year by various PD PPPs.¹³ Public and private sectors in some developing countries are also working to build innovative capacities through the establishment of IP management systems, drug and vaccine manufacturing facilities, and regulatory capabilities.

Some developing countries are more scientifically advanced and have the greatest capacity to discover, develop, manufacture, ensure safety, and market new health products. Innovation can occur in any locality, and this paper highlights recent dramatic progress in a few countries.¹⁴

Mashelkar has introduced a construct for understanding the special category of IDCs (Table 1).¹⁵ ¹⁶. He writes (for the full paper, see page 16-32 in this volume of *Innovation Strategy Today*):



Table 1: Economic strength and innovation capability

		Low	High
		Innovation Capability	
Economic Strength	High	I	II
	Low	III	IV

Adapted from Mashelkar 2005.¹⁵

“We can, in a simple-minded way, position all the countries in a single diagram in terms of their relative economic strength and indigenous capacity in science and technology (Table 1). In the top right-hand corner are such developed nations as the USA, Japan, countries in Europe, etc. They have a very high indigenous science and technology capacity and a very high economic strength. In contrast, in the lowermost left-hand quadrant are the least developed countries, including those in sub-Saharan Africa, where indigenous science and technology capacity as well as economic strength are low. In the top left-hand quadrant are countries that have attained very high economic strength by the strength of their natural resources (such as the oil rich Middle East countries). But these do not have any significant indigenous science and technology capacity. The most interesting quadrant is the lower right-hand area. These countries have high indigenous science and technology capacity but relatively low economic strength. They include India, China, Brazil, Argentina, Chile, South Africa, etc. Of course, the positions of developing nations in this diagram are not static. Different countries in different times of history occupied different positions on this map. For instance, not too long ago, Korea belonged to the lower right-hand quadrant. But they moved upwards to attain the status that OCED countries enjoy today.”

While economic strength is easily measured, and reasonably well-understood, innovation capability presents more difficulty. Given the complex set of activities involved in the innovative process, measurement of “innovative capability” must be based on several indicators. Cross-country comparative data for a broad set of measures are limited. One often used measure of innovation is the number of US pat-

ents issued.¹⁷ Innovative efficiency, by extension, may be measured by the number of US patents per GDP/capita. Patents do not necessarily translate into products, and US patents represent only a subset of all innovation in a country. Thus, while instructive, this is an indirect measure of innovation capability. However, because of the global dominance of US markets, it has the advantage of creating a common yardstick against which to measure all countries.

Table 2 shows the top 25 countries in the world by rank order, analyzed for all US patents issued where at least one inventor is from the subject country. Several IDCs, indicated by shading, appear in the table. Note that India and China are at 3rd and 4th places. Other developing countries on the list are Brazil, South Africa, Thailand, Argentina, Malaysia, Mexico and Indonesia (in rank order).

Table 2: US patents, GDP per capita, and US patents per GDP/capita (2003)

	Country	US Patents	GDP per capita	US patents per GDP per capita
1	USA	99,386	36,006	2.760
2	Japan	37,779	31,407	1.203
3	India	444	487	0.912
4	China	724	989	0.732
5	Germany	13,110	24,051	0.545
6	Korea, Rep.	4,246	10,006	0.424
7	France	4,682	24,061	0.195
8	Canada	4,410	22,777	0.194
9	UK	4,803	26,445	0.182
10	Italy	2,206	20,528	0.107
11	Israel	1,392	15,792	0.088
12	Brazil	209	2,593	0.081
13	Sweden	1,771	26,929	0.066
14	South Africa	142	2,299	0.062
15	Australia	1,174	20,822	0.056
16	Switzerland	1,845	36,687	0.050
17	Belgium	998	23,749	0.042
18	Finland	1,009	25,295	0.040
19	Austria	753	19,749	0.038
20	Thailand	64	2,060	0.031
21	Argentina	76	2,797	0.027
22	Singapore	564	20,886	0.027
23	Malaysia	95	3,905	0.024
24	Mexico	129	6,320	0.020
25	Indonesia	16	817	0.020

Source: US Patents: www.uspto.gov
GDP per capita: www.worldbank.org



The productivity of IDCs is a relatively new phenomenon which may have contributed to the relative lack of attention it has received. Figure 1 shows the growth in numbers of US patents by inventors from several IDCs^a from 1990 through 2003 where the words “drug”, “vaccine”, or “pharmaceutical” appear in the patent abstract.¹⁸ The rate of patenting was relatively constant during the first half of the 1990s, but accelerated dramatically since 1996.

Figure 2 compares the two most active patenting IDCs, China and India, with Korea. Korea has been an OECD country since 1995 and is often used as a benchmark for developing countries because its GDP per capita has grown exceptionally rapidly since 1960¹⁹.

Citations of published articles are another proxy indicator of innovative capacity. A recent analysis by King²⁰ of highly cited publications from 1993-1997 and 1997-2001 also suggests a rapid increase in capabilities in IDCs. Comparing the two periods of the

study, several IDCs increased the number of highly cited papers significantly and either exceeded or equaled the average percent increase in highly cited papers of all countries that were analyzed (Table 3).

Comparing the efficiency of countries (publications per GDP/capita) shows that the top ten countries in the world (in rank order) are India, China, United States, Brazil, Germany, United Kingdom, Japan, South Africa, Canada, and Italy.

Table 3: Numerical and Percent increases in the number of papers among the 1% most highly cited papers

Country	Numerical increase	Percent increase
Brazil	88	88%
China	218	145%
India	93	83%
South Africa	30	59%
Top 30 countries average	112	59%

Figure 1: US patents from selected countries. Patents are for drugs, or vaccines or pharmaceuticals (Countries included are Argentina, Brazil, China, India, Malaysia, Mexico, South Africa, and Thailand)

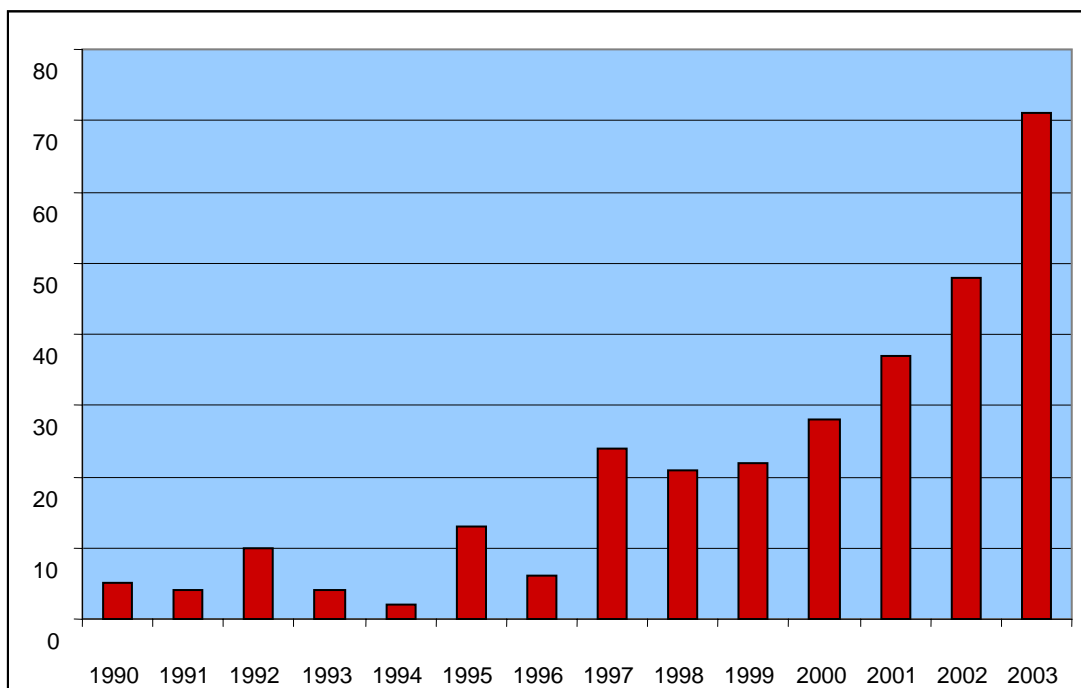
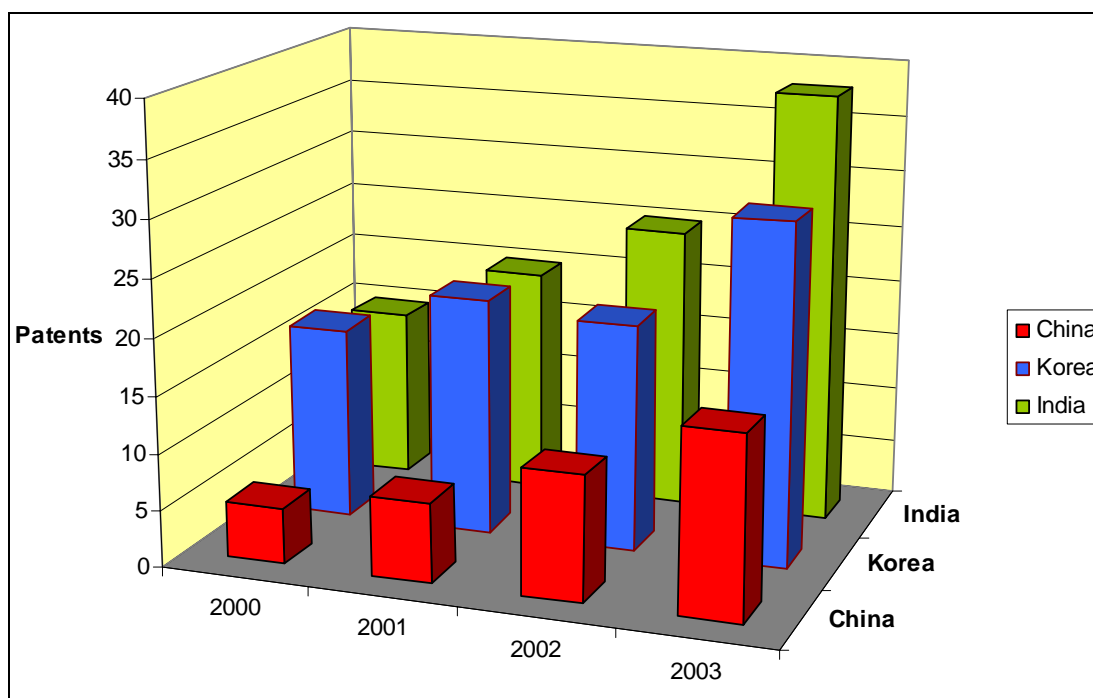


Figure 2: US drug, vaccine, or pharmaceutical patents by inventors from China, Korea and India



It is likely that for many of the IDCs, the impressive trends in patents and citations are a result of the recent and rapid increases in R&D investments, preceded by longer-term investments in science and engineering education. According to a 2001 study, in 1998 Argentina, Brazil, Costa Rica, Cuba, India, Malaysia, Mexico, Panama, Peru, the Philippines, Thailand, and Turkey spent a minimum of \$2.3 billion for health research for national needs.²¹ This number could be compared with the budgets of the UK Medical Research Council (\$0.3 billion) and the US National Institutes of Health (\$13.647 billion) in 1998. Notably, this figure does not include China for which data were not available. In developed countries the public and private sectors invest comparable amounts in health research, whereas in most developing countries the majority of health research is supported by the government and conducted in public institutions.

Each of these countries, including China, is committed to double digit percent increases in health research funding.^{22,23} We estimate total allocations in 2004 at no less than \$3 billion. For the fiscal year beginning April 2005, the Indian government alone

plans to increase spending in all R&D to \$3.3 billion, implying a minimum 15 percent increase in all major projects.²⁴ The private biotechnology industry in India projects investments of \$10 billion by 2010.²⁵ Some developing countries are aggressively creating high quality pharmaceutical and biotechnology industries on their own initiative.^{26,27} There is also rapidly growing capability to conduct clinical trials according to good clinical practices standards²⁸.

Manufacturing and markets in developing countries are important components of innovation systems. There is limited but growing evidence that IDC firms, if well networked and set up efficiently, are able to achieve significant cost advantages in production.²⁹ For example, a recent study by the Organization of Pharmaceutical Producers of India found a cost advantage of up to 50 percent compared with the United States.³⁰ Further analysis is needed, and cost advantages may differ significantly between drug and vaccine manufacturers, but developing country cost-advantages arguably could lead to lower prices for products directed to the poor. South-South trade in low-cost products is an important aspect of access by the poor to both new and existing health interven-



tions. By value, 67% of India's drug exports, 74% of Brazil's and 92% of Argentina's go to other developing countries, while 63% of Uganda's drug imports and 54% of Tanzania's drug imports by value come from other developing countries.³¹

By volume, India is now the fourth largest producer of pharmaceuticals in the world (13th by value), the country holds 8% of the global pharmaceutical market by volume (1% by value), and India has the largest number of manufacturing facilities approved by the US Food and Drug Administration (FDA) anywhere outside of the United States.³² According to a recent analysis by the UK Department for International Development (DFID),³³ China is now the 10th largest pharmaceutical market after Mexico (9th), and the second largest producer of pharmaceutical ingredients in the world. For penicillin, vitamin C, tetracycline, doxycycline and cephalosporin, China is the largest producer in the world. The Serum Institute of India is now the largest manufacturer of diphtheria-pertussis-tetanus (DPT) vaccine in the world.

According to the DFID study, 60% of UNICEF's vaccine requirements for the Expanded Programme on Immunization (EPI) are produced in just four countries: India, Indonesia, Cuba and Brazil. Thailand obtains 90% of its antiretroviral (ARV) ingredients from India, while the three South African producers of ARVs obtain 100% of their raw materials from India.

*"The Thai Public Health Ministry has clearly stated that their ambitious antiretroviral treatment programme would not exist without generic drugs, which would not have been possible without Indian [active pharmaceutical ingredient] supply. ...Similarly, data from the Brazilian firm, Farmanguinhos, which supplies approximately 40% of the total [Brazilian] Ministry of Health ARV demand, shows that approximately 74% of total ARV purchases in 2002 and 94% of total ARV purchases in 2003 were supplied by Indian, Chinese and Korean firms."*³⁴

A recent supplement of *Nature Biotechnology*²⁷, contains several papers emerging from a three-year seminal study by the Canadian Program on Genomic

and Global Health at the University of Toronto.²⁷ The papers contain numerous examples of the growth of health innovation in developing countries. For example, the number of exhibitors from developing countries attending the US Biotechnology Industry Organization's annual conference grew from 2 in 2001 to 97 in 2004. In late 2003, the Chinese firm Shenzhen SiBono GenTech became the first in the world to obtain a license for a recombinant gene therapy product. South Africa's Council of Scientific and Industrial Research (CSIR) has isolated a hunger-suppressing steroidal glycoside (P57AS3) from an indigenous plant, *Hoodia gordonii*, and licensed the product to the British biotechnology firm, Phytopharm. The Synthetic Antigen Laboratory at the University of Havana played a leading role in developing the world's first human vaccine with a synthetic antigen. The vaccine protects against *Haemophilus influenzae* infection, which often leads to pneumonia and meningitis in children under the age of 5. Made with a chemically produced antigen instead of fermented bacterial culture, it is much cheaper to produce and safer than vaccines coming from living organisms.

Despite these impressive developments affecting innovation capabilities in developing countries, many impediments remain. *The Economist*,³⁵ reporting on the University of Toronto study, summarized some of specific problems in IDC health innovation systems:

"Brazil needs better links between academia and industry. Egypt's budding biotechnologists are short of cash from both government and private sources. India's regulatory system is slowing down product development. South Africa needs to do more to reverse its brain drain, and train more researchers to boost their ranks."

It is these impediments, and others, that an initiative focusing on innovation in developing countries will help to address. Networking among developing countries is needed to share information and good practices for better alignment of national innovation policies and national health priorities. Such an initiative will be essential if the growing health innovation capability of developing countries is to have an impact on public health.



Is Health Innovation in Developing Countries likely to Strengthen the Fight Against Diseases of the Poor?

There is as yet insufficient understanding of the detailed nature, dimensions, trajectory, and potential impact of the revolution of innovation in developing countries, of whether and how this revolution can best address the needs of the poor. Presumably, a significant portion of public sector investments by developing countries in health research is based on national health priorities. These financial allocations require more in depth analysis to understand how they are being used, but it is clear that these countries are allocating large and increasing sums thereby providing the opportunity to allocate increasing amounts to research on diseases of the poor.

As emphasized by a recent UN Commission,³⁶ the role of the private sector in IDCs will be critical to success. Will it be possible to obtain their commitment, to a meaningful extent, to working on diseases of the poor? Most of the PD PPPs referred to earlier collaborate with pharmaceutical companies in developed countries, but none of these companies have prioritized diseases of the poor.³⁷ The amount of in-house funds spent on diseases of the poor is insignificant compared to what is spent on their lead candidates—for cardiovascular, cancer, chronic diseases.³⁸ Prioritizing the disease and health concerns of lucrative markets, for patients in the developed world, is understandable given all companies' drive to maximize return-on-investment.^{39, 40}

In one documented case, a major product development PPP, the Meningitis Vaccine Project—a collaboration between WHO and the Program for Appropriate Technology in Health (PATH)—was able to forge a collaboration with an IDC manufacturer to produce an affordable meningitis conjugate vaccine for sub-Saharan Africa.⁴¹ After extensive consultations with African health officials, the Meningitis Vaccine Project sought to develop a product at a price not to exceed \$1.00 per dose. Multinational manufacturers were not interested in participating in this project.

According to the previously cited Indian private biotechnology investment projections, the R&D based

private sectors in IDCs (as opposed to generics and material manufacture) are growing rapidly. It is critical to recognize that all of these companies are driven to maximize a return on investment. It is not surprising, then, that recent studies show that many of these companies are according priority to “diseases of the rich,” both locally and abroad.³⁷ For example, in the patent data cited above, for all IDCs in 2003 only 10 of 105 drug, vaccine, or pharmaceutical patents issued were for diseases that predominantly affect the poor (three antivirals, one anti-malarial, two antibiotics for drug-resistant bacteria, two vaccines, and one treatment for vaginal infections).

However, some IDC companies are considering business strategies that include diseases of the poor, and there are reasons to speculate that—given their apparent cost and location advantages—they might be better placed to turn diseases of the poor into profitable business opportunities.⁴² For example, the offer noted above by the meningitis program made good business sense to an Indian manufacturer but not to multinational manufacturers. In addition, an Indian biotechnology company, Lupin, has formed a PPP with the Council for Scientific and Industrial Research to push forward a TB drug⁴³. The University of Toronto study of health biotechnology innovation systems in seven developing countries found that health biotechnology in IDCs was often focused on local health needs, including import substitution (with lower cost products), manufacturing process improvements, and novel invention²⁷.

Many IDC firms are now forming joint ventures with major international companies. Examples include an R&D partnership between Ranbaxy Laboratories (India) and GlaxoSmithKline for product identification⁴⁴ and, in Latin America, partnerships between Biomanguinhos/FIOCRUZ (Brazil) and Glaxo SmithKline for the production of *Haemophilus influenzae* vaccine, the Instituto Butantan (Brazil) and Aventis Pasteur for influenza vaccine, and the Instituto Finlay (Cuba) and Glaxo SmithKline for meningococcal group B vaccine.⁴⁵



The Study of Health Innovation Systems

Scholars who study innovation systems have, until very recently, paid little attention to health. However, Dhar and Rao have recently examined the development of the pharmaceutical industry in India.⁴⁶ Their analysis identified key determinants of innovation.

- *Support for R&D.* The government provided extensive subsidies for R&D including tax concessions, soft loans and exemptions from price controls. The government also provided extensive support of government research centers such as for the Council for Scientific and Industrial Research that actively engage in collaborative projects with private industry. Beginning in the 1990s, the government developed policies to stimulate local public-private R&D partnerships for product development⁴⁷.
- *Manufacture.* Until 1994, government policy required firms that were not using high technology in production of bulk drugs or formulations to limit their foreign holdings to 40 percent to be considered Indian firms.
- *Intellectual property.* The Indian system recognized only process patents, excluding product patents for pharmaceuticals and agricultural chemicals from IP monopoly protection.
- *Domestic markets and exports.* This system allowed manufacturers to reverse engineer products that had been developed in the North—both on and off patent—for the domestic market. Patented products could then enter international commerce as soon as the relevant patents had expired.

The University of Toronto study²⁷ identified the following main features of innovation.

- *Government policy:* Proactive role and long term support for targeted R&D. Establishment and management of policies on intellectual property rights and drug regulation. Establishment of policies for addressing brain drain problems, encouraging private sector development.
- *Public research institutes:* The growth of scientific institutions with highly trained staff, increasing number of paper published in international peer reviewed journals, capability to produce high quality products, formation of various close linkages and partnerships among themselves and with the health system and the private sector, and development of products.
- *Industry:* The growth of private enterprise as reflected by increasing number of biotechnology firms, percent of the domestic market supplied by local firms, size of the domestic market, number of patents, and active knowledge flow and partnerships with the other parts of the innovation system.
- *The general public:* The receptivity of and support by the public to modern biomedical research particularly with respect to R&D involving genetics.

These findings, as well as those of Da Motta e Albuquerque and Cassiolato⁴⁸, indicate that there are key determinants of health innovation systems in developing countries, and that strengthening these systems can help address national health priorities.

A Framework for understanding Health Innovation Systems

In order better to understand health innovation systems in developing countries,¹⁰ and maximize their ability to address diseases of the poor, we propose a framework with six determinants.^{9,49, 50, 51}

- Creating capacity for and undertaking R&D
- Creating and sustaining capabilities to manufacture products to appropriate standards
- Promoting and sustaining domestic markets
- Promoting and sustaining export markets
- Creating and implementing systems for IP management
- Creating and implementing systems for drug, vaccine, diagnostic and device regulation



Table 4 shows these six determinants in a framework that illustrates how developing countries can progress in innovation capability⁵². An essential aspect of this framework is that the six determinants are assumed to be dynamically linked such that progress in one is facilitated by and dependant upon progress in the others.⁵³ Similarly, the lack of progress in one can impede progress in the other five. Therefore, if a country wishes to improve its innovation capabilities, it must make coordinated, dynamic progress in all of the determinants.

For example, it will be difficult to create an export market without a satisfactory national drug regulatory system. Similarly, (and obviously) it will be difficult to develop new products from public or private R&D without a domestic ability for high quality manufacturing.

Publicly funded research also depends on sound public-private partnerships—which ideally protect the public interest—to translate academic findings into high quality products.^{54, 55} Finally,

Table 4: Stages of health innovation capabilities in developing countries by six determinants (Capabilities in developed countries are shown for comparison)

	Manufacture	Domestic Market	Export Market	R&D	IP System	Drug Regulatory System
Stage 1	Assembly of imported components	Small market	Very little except as toll manufacturer	Very little	Very limited understanding of IP; no IP protection	Very limited
Stage 2	Production on license or by copy with significant cost-advantages over Northern products	Growing domestic market of increasing interest to foreign companies; some import substitution; significant share of imports come from other developing countries	Growing trade; companies learning how to establish export markets; significant share of exports go to other developing countries	Local government and foreign donor-funded R&D to understand technology either to produce on license or to copy	Patents allowed for local inventors, but foreign inventors and investors still not interested because of lack of markets and IP protection; few local public-private partnerships (PPPs)	Limited services without enforcement capabilities
Stage 3	Manufacture of domestically developed high technology products with significant cost-advantages over Northern products; growing source of outsourcing	Rapidly growing domestic market of interest to foreign companies	Increasing exports make significant contribution to GNP; significant share of exports go to other developing countries	Scientifically advanced; funded predominantly by local government, and carried out predominantly by local public research institutions; capable of innovation	Advanced IP system, but poorly enforced; moderate experience with technology management in local PPPs	Advanced capabilities but not at highest level because of need to strengthen capabilities as appropriate
Developed countries	Most developed capabilities to produce high technology drugs, vaccines, and devices	Highly profitable market in both the public and private sectors generating profits to support, in part, advanced research	Global companies	Generous support for health research from basic to applied. Large research investment by private companies including large pharmaceutical manufacturers and biotechnology companies	Established system of IP protection, and management of technology in local PPPs (e.g., university-industry R&D agreements)	A dedicated agency overseeing regulatory approvals of drugs/vaccines. In addition, the government oversees clinical trials & production facilities and enforces rules and regulations.



IDCs need to develop intellectual property systems that can attract private investment and through ethical stewardship can address public health needs.

Experience from non-profit product development partnerships shows that IP rights can be used by the public sector to help attract private sector interest, mobilize the necessary funds, and ensure affordability and access to essential new health products. There is therefore a need for special care in the development of national IP systems. The most appropriate IP system for IDCs at different stages of develop-

ment, particularly when viewed with a focus on diseases of the poor, remains an open question for policy research. This point has been raised by many commentators, perhaps most notably by the UK Commission on Intellectual Property Rights⁵⁶ and a recent major study by the World Bank⁵⁷. On 1 January 2005 the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) went into effect for most developing countries. The impact of TRIPS on innovation is a matter of great debate and there is a need to study this impact especially with respect to innovation of health products needed by the poor.

A Network to Strengthen Developing Country Capabilities

In the complex field of new health product innovation, national governments, public and private sector product development efforts, and other related initiatives need to develop a coherent strategy for product development by addressing each of the determinants discussed above. Some IDCs may be able to address, and will address, all the determinants themselves. However, in other cases strategies involving coordination and learning among countries may be the best route. South-South information exchanges could help countries learn from one another to maximize the effectiveness of their health innovation systems to both achieve economic development and to address national health priorities, including diseases of the poor.

Developing countries with innovation capabilities could take on an important role of leading the global advocacy for health product innovation by sharing experiences, shaping priorities, developing workable strategies, conducting collaborative programs, and facilitating public-private collaborations. Such efforts would complement other initiatives including the PD PPPs which are primarily headquartered in developed countries (with numerous collaborative relationships in IDCs).⁵⁸

A South-South based initiative could help to promote research on health innovation systems (a heretofore neglected field), support the dissemination of information about effective innovations sys-

tem policies among IDCs, promote the conduct of demonstration projects of innovation system policies concerning one or more of the determinants, and provide a forum for IDCs to exchange information about health innovation systems. There is a need to mobilize relevant institutions in developing countries that are concerned with health innovation including R&D centers, technology and IP management centers, drug and vaccine manufacturers, sources of financing, regulatory bodies, and government institutions and non-governmental organizations that are concerned with access to health products and services.

As a mechanism to help strengthen health innovation systems in developing countries, this is consistent with key recommendations of previous studies that have examined the potential role of developing countries in health product innovation. The Evans Commission of 1990 highlighted that, in addition to addressing their own health needs, developing countries could contribute to the solution of global health problems.⁵⁹ The UK Commission on Intellectual Property Rights has examined the issue of the participation of developing countries in health product innovation.⁶⁰ The Commission's report notes,

"[Of important promise] might be a network of the public-private partnerships in developing countries, taking advantage of the concentration of research resources in



public sector institutions but also the opportunity to build research capacity in the private sector.” It then goes on to recommend:

“Public funding for research on health problems in developing countries should be increased. This additional funding should seek to exploit and develop existing capacities in developing countries for this kind of research, and promote new capacity, both in the public and private sectors.”

There are efforts underway to link and mobilize innovation in developing countries. For example, the Global Forum for Health Research supports an annual meeting to bring together key individuals and organizations concerned with research on priority health problems in developing countries⁶¹ while the WHO-hosted Tropical Disease Research Special Programme has been a leader in this effort, and an ‘incubator’ of PD-PPPs.⁶² The Global Research Alliance (GRA), composed of nine research institutes in developed and developing countries, seeks to facilitate and promote research in a number of development areas including health.⁶³ The Research Agency Collaborative for Global Health (REACH) is an emerging initiative to facilitate coordination and collaboration among national medical research agencies in both developed and developing countries.⁶⁴ This year, the WHO, along with nine developing countries, created and launched the National Regulatory Network for Vaccines. The participating countries are Brazil, China, Cuba, India, Indonesia, Russia, South Africa, South Korea and Thailand.

Some new efforts have been created for, and led exclusively by, developing countries themselves. Each of these could be an important contributor to an international network promoting health product innovation in developing countries:

- The Asia Pacific Economic Cooperation (APEC) is developing a comprehensive Strategic Plan for its Life Sciences Innovation Forum that addresses the issues raised in this paper.⁶⁵
- India-Brazil-South Africa Dialogue Forum (IBSA), established in June 2003, includes a focus on intel-

lectual property and access to medicine, traditional medicine, and research and development of vaccines and pharmaceutical products to address national health priorities.

- Technology Network for HIV/AIDS, announced during the 2004 Bangkok meeting on HIV/AIDS, includes Brazil, China, Nigeria, Russia, Thailand and Ukraine (and possibly South Africa and India in the near future). The Network will support research and South-South technology transfer on antiretroviral drugs and drug formulations, and the development of an HIV vaccine.
- Developing Country Vaccine Manufacturers’ Association, established in 2000.⁶⁶
- The Third World Academy of Sciences, whose goal is “to promote scientific capacity and excellence for sustainable development in the South.”

However, based on the analysis presented here, something more comprehensive seems to be needed. The new initiative for health innovation systems in developing countries could help promote:

- research on health innovation systems;
- information sharing among IDCs;
- information dissemination on effective policies and practices;
- demonstration projects; and
- capacity building to support all the above points.

A major goal would be to help formulate policies in several areas including financing, capacity building in each of the determinants, and the formulation of laws and government regulations to promote health innovation.

Innovation systems research

There is a real need to encourage studies focusing on diseases of the poor. There is a need for innovation system theorists and global health practitioners to develop a more sophisticated literature on health innovation in developing countries. Methodologies for country, product and company case studies, derived from innovation systems theory, need to be applied



to health innovation. This work would evaluate best policies and practices for consideration by IDCs. Another important product of this work would be the development of sustainable and consistent networks for information collection, analysis and sharing.

Information dissemination

There is a need to ensure the widest possible dissemination of best practices and policies identified through research and forum activities (see below) by, for example, codifying the output of innovation research into briefs for policy makers and practitioners.

Demonstration projects

There is a need to support demonstration projects to test implementation of proposed policies and practices in real life situations, and to determine how best practices and policies may vary depending on local conditions.

A Forum for IDCs

These activities could be addressed to improve the efficiency and effectiveness of health innovation systems in IDCs through a forum that would bring together diverse institutions and individuals, including scientists, policy makers, and leaders from international development and the private sector. Forum participants would:

- discuss specific innovation determinants and share experiences related to innovation in health products, drawing on the health innovation research activities;
- develop consensus on best practices and policies; and
- advance policy initiatives to improve the efficiency and effectiveness of health product innovation.

Conclusions

To address global health disparities, the global community must harness the potential of national and regional health innovation systems throughout the world, with a particular focus on the development of technologies and techniques that are relevant to developing countries.⁶⁸ This means making full use of

In 2003, The WHO Commission on Macroeconomics and Health called for an expanded outlay in 2007 of approximately \$1.5 billion per year in R&D through a new Global Health Research Fund (GHRF).⁵⁹ These funds would be in addition to those already allocated to existing channels such as the WHO-based research programs on tropical diseases and human reproduction, and the PD PPPs. The report states, "A key goal of the GHRF would be to build long-term research capacity in developing countries themselves. The GHRF would provide vital funding for research groups in low-income countries."⁵⁹ Unfortunately, developed countries have not implemented this recommendation perhaps, in part, due to a lack of appreciation of how rapidly capabilities for innovation in developing countries are growing.

Arguably, those closest to the needs of the poor are the communities, scientists, policy makers, and institutions—public and private—in the countries where the challenges of poverty reside. As persuasively argued by Lucas,⁶⁷ it is essential to devise ways in which programs in developed countries can become better integrated with the scientific and technological institutions in developing countries that have been rapidly expanding their ability to undertake health innovation and are becoming part of the global knowledge economy.

Solutions depend on sophisticated global partnerships and collaborations to share knowledge and good practices in innovation policies to enable developing countries to drive and own agendas and harness their available capabilities to achieve the most effective ends including the improved health for the poor, and the generation of wealth.

abilities, energy and resources in both developed and developing countries. IDCs should assume a leadership position in health innovation, both because of their increasing capacity to address global health problems, and because they are literally closer to the legitimate voices of those living in poverty. A new



focus on health innovation systems in developing countries should capture the imagination of those in leadership positions and many others who share the

belief that all people, especially the disadvantaged, should be able to share equitably in the benefits of modern health innovation.

Notes and References (all web pages have last been accessed on 16 April 2005)

- ¹ www.undp.org/mdg
- ² See report of Global Commission on Macroeconomics and health. www.cmhealth.org
- ³ Statistical annex, *World Health Report 2004* www.who.int/whr/2004/en
- ⁴ Morel CM. "Neglected diseases: under-funded research and inadequate health interventions. Can we change this reality?" *EMBO Rep.* 4 Spec No: S35-S38, 2003.
- ⁵ Black RE, Morris SS, Bryce J. "Where and why are 10 million children dying every year?" *Lancet* 2003; **361**: 2226-34.
- ⁶ Yach D, Hawkes C, Gould CL, Hofman KJ. "The global burden of chronic disease: overcoming impediments to prevention and control." *JAMA*. June 2, 2004. Vol 291, No. 21. pp 2616-2622.
- ⁷ Kettler H, White K in consultation with Jordan S. "Valuing Industry Contributions to Public-Private Partnerships for Health Product Development." The Initiative on Public-Private Partnerships for Health, Global Forum for Health Research, Geneva, 2003. www.ippph.org/index.cfm?page=/ippph/publications&thechoice=retrieve&docno=35
- ⁸ www.globalforumhealth.org
- ⁹ See, for example: Lall S. "Indicators of the Relative Importance of IPRs in Developing Countries." Issue Paper No. 3. *Intellectual Property Rights and Sustainable Development*. UNCTAD-ICTSD Project on IPRs and Sustainable Development. June 2003.
- ¹⁰ Mahoney RT. "Determinants of Innovation: A Proposed Framework." Bellagio meeting on Accelerating Product Development and Ensuring Product Access for Diseases of Poverty: The Role of Public-Private Partnerships in Developing Countries. May 10-13, 2004
- ¹¹ "Health Biotechnology Innovation in Developing Countries," *Nature Biotechnology*, Volume 22 supplement, December 2004.
- ¹² www.globalforumhealth.org/filesupld/109004_chap_5.pdf. p. 116. 2004.
- ¹³ Estimate by Gardner CA, an author of this paper.
- ¹⁴ The term "IDC" came into use during a meeting in Bellagio, Italy, attended by most of the current authors in May 2004. While all developing countries can innovate, some are clearly more innovative than others and may be called "advanced IDCs."
- ¹⁵ Mashelkar, RA. 2005. "Nation Building through Science and Technology: A Developing World Perspective". (10th Zuckermann Lecture, the Royal Society, London). *Innovation Strategy Today* 1(1):16-32.
- ¹⁶ Mani has constructed a similar analytical framework in which he categorizes Mashelkar's low economic strength countries as either Type 1 or Type 2. Type 1 countries have the potential to create new technologies themselves as measured by numbers of US patents issued to inventors from those countries. Type 1 countries are equivalent to what we call IDCs.
- ¹⁷ See for example: Nelson, Richard R (ed.). *National Innovation Systems*. Oxford University Press, Oxford, New York. 1993. p. 303.
- ¹⁸ www.uspto.gov
- ¹⁹ Nelson RR and Pack H. *The Asian Miracle and Modern Growth Theory*. World Bank Working Papers Series No. 1881. October 1997.
- ²⁰ King DA. "The scientific impact of nations: What different countries get for the research spending." *Nature* **430**, 311-316 (2004).
- ²¹ *Monitoring the Financial Flows of Health Research*. Global Forum for Health Research. Geneva, Global Forum for Health Research, 2001.
- ²² *The 10/90 Report on Health Research 2003-2004*. Global Forum for Health Research (2004). Geneva. 282 pages.
- ²³ Massarani L, 2004. Brazil seeks UNESCO's aid on science funding bid. 19 May 2004 www.SciDev.Net
- ²⁴ Jayaraman KS. "Indian scientists welcome broad increase in funding." *Nature*. **430**, 281 (2004).
- ²⁵ Madhavan N. "India targets \$10 Bln in Biotech." *Reuters*. July 11, 2004.
- ²⁶ "Interim Report of Task Force 10 on Science, Technology and Innovation." February 1, 2004. *Millennium Project of the UN Secretary General and the UN Development Group*. www.unmillenniumproject.org
- ²⁷ "Health Biotechnology Innovation in Developing Countries," *Nature Biotechnology*, Volume 22 supplement, December 2004.
- ²⁸ Stevens W. Good clinical laboratory practice (GCLP): the need for a hybrid of good laboratory practice and good clinical practice guidelines/standards for medical testing laboratories conducting clinical trials in developing countries. *Qual. Assur.* 2003. Apr.-May 10(2). Pp. 83-9.
- ²⁹ McKelvey M et al. (eds.). *The Economic Dynamics of Modern Biotechnology*, Cheltenham, UK: Edward Elgar. 2004
- ³⁰ *Outsourcing Opportunities in Indian Pharmaceutical Industry*. Organisation of Pharmaceutical Producers of India. OPPI & Monitor Company Group LP, pp. 24-25. Bombay. 2003.
- ³¹ Bale HE. "Consumption and trade in off-patented medicines." CMH Working Paper Series, No. WG 4: 3, WHO Commission on Macroeconomics and Health, May 2001, p. 19. www.cmhealth.org/docs/wg4_paper3.pdf
- ³² *Outsourcing Opportunities in Indian Pharmaceutical Industry*. Organisation of Pharmaceutical Producers of India. Bombay. 2003



- ³³ Grace C. "The effect of changing intellectual property on pharmaceutical industry prospects in India and China: considerations for access to medicine," Issues Paper, Health Systems Resource Centre, Department of International Development, United Kingdom, June 2004.
- ³⁴ Ibid.
- ³⁵ "Third-World Biotechnology: Southern comfort, Eastern promise." *The Economist*, December 11, 2004, p. ??
- ³⁶ "Commission on the Private Sector & Development. Unleashing entrepreneurship: making business work for the poor." United Nations Development Programme. New York. 2004.
- ³⁷ Kettler H and Modi R. "Building local research and development capacity for the prevention and cure of neglected diseases: the case of India." *Bull. WHO*. 2001, 79(8). pp 742-747, 2001.
- ³⁸ Novartis has established a major research center in Singapore concerned with dengue and tuberculosis but the activities are mainly laboratory studies and not product directed. GlaxoSmithKline has a dedicated drug discovery unit in Tres Cantos, Spain which leads drug discovery initiatives in malaria and tuberculosis. science.gsk.com/about/disease.htm
- ³⁹ Trouiller P, Torreele E, Oliaro P, White N, Foster S, Wirth D, Pecoul B. "Drugs for neglected diseases: a failure of the market and a public health failure?" *Trop. Med. and Intl. Health*. 6(2), Nov. 2001. pp. 945-951.
- ⁴⁰ Kettler H and Towse A. "Public private partnerships: A report for the WHO Macroeconomic Commission on Health." www.cmhealth.org
- ⁴¹ Jodar L, LaForce FM, Ceccarini C, Aguado T. and Granoff D. "Meningococcal conjugate vaccine for Africa: a model for development of new vaccines for the poorest countries." *Lancet*. image.thelancet.com/extras/02art7254web.pdf
- ⁴² Prahalad CK. "The Fortune at the Bottom of the Pyramid: Eradicating Poverty through Profits." Wharton School Publishing. Upper Saddle River. 399 pages. 2005.
- ⁴³ www.businessworldindia.com/sep0604/news03.asp
- ⁴⁴ www.ranbaxy.com/newsroom/pressrelease_det.asp?sno=131
- ⁴⁵ www.paho.org/english/gov/ce/ce130-10-e.pdf
- ⁴⁶ Dhar B, Rao NC. Transfer of Technology for Successful Integration into the Global Economy. A Case Study of the Pharmaceutical Industry in India. UNCTAD/UNDP. New York and Geneva. 2002.
- ⁴⁷ Saha R, Satyanarayana K, and Gardner CA. "Building a 'Cottage Industry' for Health (and Wealth): The New Framework for IP Management in India." *IP Strategy Today* 10-2004, pp. 23-58.
- ⁴⁸ Da Motta e Albuquerque and Cassiolato JE. "Less-developed countries and innovation in health: notes and data about the Brazilian case." CEDEPLAR/FACE/UFMG. Belo Horizonte. 2001.
- ⁴⁹ Mahoney RT, Lee K, Yun MK. "IP, drug regulation and building innovation capability in biotechnology: the case of Hepatitis B in Korea." Manuscript. 2004.
- ⁵⁰ Casper and Kettler A. "National Institutional Frameworks and the Hybridization of Entrepreneurial Business Models: The German and UK Biotechnology Sectors", *Industry and Innovation*, Vol 8. 2001.
- ⁵¹ Malerbo F, et al (forthcoming), *Sectoral Systems of Innovation: Concepts, Issues and Analyses of Six major Sectors in Europe*, Cambridge University Press.
- ⁵² Lee, WY. *The Role of Science and Technology Policy in Korea's Industrial Development*, Technology, Learning and Innovation. Kim L and Nelson R (eds.). Cambridge University Press, Cambridge. 2000. 377 p.
- ⁵³ Lee K, Lim CS, Park DH. The Role of Industrial Property Rights in the Economic Development of the Republic of Korea. World Intellectual Property Organization. 2003.
- ⁵⁴ Saha R, Satyanarayana K, and Gardner CA: "Building a 'Cottage Industry' for Health (and Wealth): The New Framework for IP Management in India," *IP Strategy Today*, No. 10-2004, pp. 26-60.
- ⁵⁵ *Handbook of Best Practices for Management of Intellectual Property in Health Research and Development*, published by the Centre for Management of Intellectual Property in Health Research and Development, Oxford UK, Ed. Richard T. Mahoney, pp. 129-140, November 2003
- ⁵⁶ Commission on Intellectual Property Rights. Integrating Intellectual Property Rights and Development Policy. London, September 2002.
- ⁵⁷ Fink C and Maskus K, eds, *Intellectual Property and Development*, the World Bank/ Oxford University Press, 2005.
- ⁵⁸ Fraser CM. "An uncertain call to arms." *Science* **304**, 359 (2004).
- ⁵⁹ *Health Research: Essential Link to Equity in Development*, Commission on Health Research for Development (1990). New York: Oxford University Press. 136 pages.
- ⁶⁰ "Integrating Intellectual Property Rights and Development Policy." Commission on Intellectual Property Rights. London, September 2002. p. 34.
- ⁶¹ www.globalhealthforum.org
- ⁶² Morel CM. Reaching maturity - 25 years of the TDR. *Parasitol.Today* 16:522-528, 2000.
- ⁶³ www.research-alliance.net/
- ⁶⁴ Keusch G. Boston University. Personal communication. December 2004.
- ⁶⁵ Realizing Innovation and Human Capital Potential in APEC. APEC Secretariat. Singapore. November 2004. www.apecsec.org.sg/apec/publications.html
- ⁶⁶ See for example www.vaccinealliance.org/site_repository/resources/herrera.ppt
- ⁶⁷ Lucas AO. "International Collaboration in Health Research." Commission on Macroeconomics and Health Working Paper Series, Paper No. WG2:2.
- ⁶⁸ Daar AS, Thorsteinsdóttir H, Martin DK, Smith AC, Nast S, and Singer PA. "Top ten biotechnologies for improving health in developing countries." *Nat.Genet.* 32 (2):229-232, 2002.

