Asia Pacific Foundation of Canada
Fondation Asie Pacifique du Canada

January 31, 2012

CANADA-ASIA AGENDA

www.asiapacific.ca Series Editor Brian Job Associate Editor Trang Nguyen Issue 24

Rising Innovative Capacity in Asia and Opportunities for Canada:
Focus on the Biopharmaceutical Sectors in China and India

By Rahim Rezaie

There is much discussion these days that we are in a globalized and knowledge-based economy. However, it is not clear that Canada is making the necessary adjustments to adapt to contemporary realities that demand not only knowledge generation but also efficient knowledge and technological exchange at a global level. This article focuses on the closely related, and knowledge intensive, industries of health biotechnology and pharmaceuticals in key Asian markets. China, India and a handful of other countries in the region have made significant progress in life science innovation in recent decades, yet remain in need for much of what Canada possesses – knowledge, know-how, leading-edge technology and experience in delivering world-class healthcare. This article discusses public policies and business strategies that can help Canada leverage these strengths and ensure that we are part of the growth and innovation story in Asia.

Asian Innovation and Canadian Connections

Overall commitment to science and technology development, as measured by national R&D expenditure, has been growing faster in the Asia-Pacific region than in the US or Europe (see Figures 1 and 2 and Table 1), with the relative contribution for the latter two declining between 1996 and 2007.[1] Over the past two decades, China in particular has increased its R&D commitment dramatically with national R&D expenditure rising from 0.57% of GDP in 1996 to 1.5% by 2008, reaching approximately US$ 102 billion. While India's expenditures as a portion of GDP remained largely unchanged (at about 0.8%), their real R&D investments nearly doubled during the 2002-2007 period due to GDP growth – rising from approximately US$ 13 to 25 billion.[2] These investments have translated in enhanced number of researchers, a growing share of global publications, and rising patenting rates (see Table 1). The country recently announced plans to double R&D expenditures as a portion of GDP by 2017.[3]

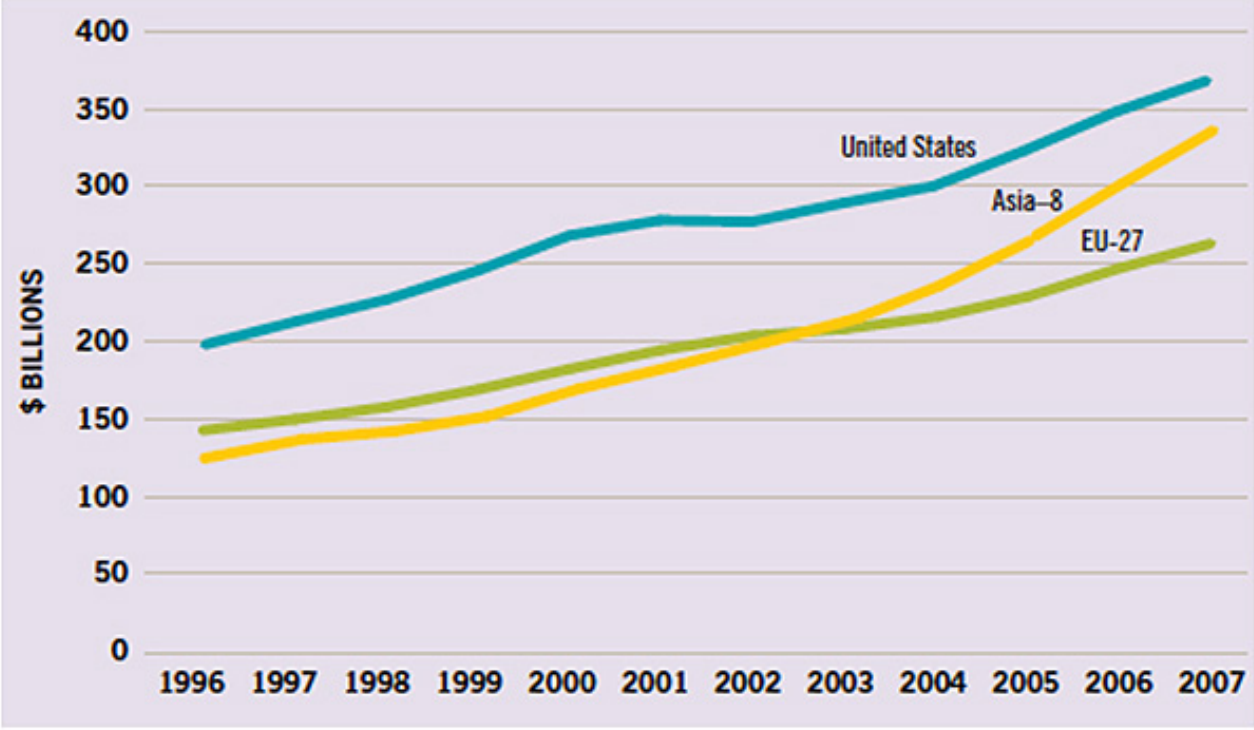
About The Author

Rahim Rezaie is a post-doctoral research fellow at the Asia Pacific Foundation of Canada and the Munk School of Global Affairs at the University of Toronto. His research over the past five years has been focused on health technology innovation within domestic enterprises in China, India and Brazil and the impact and potential of these innovations for addressing global health challenges. His current work examines the transfer of knowledge and innovations between developed and developing nations and the implications of rising innovation capacity in the emerging markets for business strategy and public policy in the industrialized world.

Figure 1. Average Annual Growth of R&D Expenditure for United States, EU-27, and Asia-8 Economies: 1996-2007

Source: Key Science and Engineering Indicators: 2010 Digest
(http://nsf.gov/statistics/digest10/nsb1002.pdf)

Figure 2. R&D Expenditures for the United States, EU-27, and Asia-8 Economies: 1996-2007



Source: Key Science and Engineering Indicators: 2010 Digest

As significant as growth has been in key Asian markets, certain sectors have far outperformed the overall economy. Two such sectors are the health biotechnology and pharmaceutical sectors (collectively referred to as 'biopharmaceutical' hereafter) in China and India (see Table 2), where double-digit growth rates have been the norm, a trend expected to continue over the coming years. Recent industry reports suggest that China's pharmaceutical market reached US$ 50 billion in 2011, making it the third largest market of its kind in the world. Credit Suisse AG estimates that China's nutritional products and drugs put together will reach US$ 110 billion by 2015, up from US$ 44 billion in 2008.[4]

The drive towards innovation results from a number of interrelated factors. These include: rapid economic growth, enhanced investments in science and technology, advancing technological sophistication of domestic industries, institutional adjustments and supports for innovation, and the rapid integration of domestic industries into the global biopharmaceutical innovation value chain. The adoption of the World Trade Organization's Trade-related Aspects of Intellectual Property Rights (TRIPS) agreement by China and India in 2001 and 2005 respectively, has enhanced the impetus to innovate by extending patent protection to pharmaceutical products. The new patent regimes diminish the ability of local firms to copy innovations made elsewhere – a common business strategy for local firms before TRIPS adoption. Together, these forces are not only re-shaping the domestic industries in China and India, they are also helping re-structure how innovation takes place within the resource-intensive global biopharmaceutical industry.

While attempts by the emerging markets to transition to innovation are often perceived abroad as posing competitive threats, these developments also present significant opportunities. This is particularly pertinent to Canada, which has a considerable focus on health research and has a vibrant biopharmaceutical industry. According to BIOTECanada, the health, medical and pharmaceutical sectors make up 63% of Canada's US$ 86.6 billion bio-economy and account for 7% of GDP.[5] The country had 532 biotech companies in 2005, employing over 86,000 people.[6] Ray et al (2009)[7] identified a total of 259 companies in 2008 that specialized in the health area and among the 181 respondents to their survey, found only 26% had collaborative linkages of any sort in the developing world as a whole. They identified 22 instances of partnerships between Canadian companies and Chinese entities and 17 cases with Indian counterparts. Therefore, Canada's engagement with Asia is not commensurate to the size of our industry and the scale and scope of emerging opportunities in Asia. Neither is our commitment reflective of our scientific strengths, where the country ranks seventh in the world in terms of number of annual scientific publications.[8]

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A Changing Innovation Landscape

China and India – and other key Asian countries such as Taiwan, Singapore and Korea – are attempting to enter the biopharmaceutical innovation landscape at a time when the nature of the game is itself evolving rapidly. Concurrent with growing innovative capabilities in these markets, the Western pharmaceutical innovation model is increasingly challenged by diminishing returns to R&D expenditures, patent expirations on blockbusters and the associated loss of revenue, and the mounting pressure on drug prices due to rising healthcare costs. According to the Pharmaceutical Manufacturers Association (PhRMA), the U.S. biopharmaceutical sector spent US$ 67.4 billion dollars on R&D in 2010[9], during which the country's Food and Drug Administration (FDA) approved only 21 new drugs,[10] continuing a declining trend that has been ongoing for over a decade. DiMasi et al (2003)[11] estimated

that the out-of-pocket costs to take a drug from discovery through marketing at over US$ 400 million, rising to over US$ 800 million (2000 dollars) when opportunity costs are factored in. These estimates factor in costs of project failures and were rising at an annual rate of 7.4% above inflation. It is increasingly clear that **the prevalent model of drug development is unsustainable.** This is particularly so if one considers affordability of products to people in the developing world. To the millions of people in the globe that live on a few dollars a day, access to many health technologies that we take for granted remains allusive. For example, it took about two decades before hepatitis B vaccine became widely available in the developing world when a process innovation by an Indian company named Shantha Biotechnics (now part of Paris-based Sanofi) drastically reduced the price through a manufacturing process innovation.

The global biopharmaceutical industry is now transitioning from firm- and country-centric innovation to a more global and network-based innovation model. The new pattern that is emerging is a globally fragmented drug development value chain with greater participation of key Asian markets. This shift to global, network-based innovation has the potential to create considerable opportunities – particularly for latecomer nations and small and medium enterprises in smaller developed markets such as Canada. It can also accelerate drug development and reduce innovation costs making end products more affordable.

Five major trends point to the growing globalization of biopharmaceutical sector and the significance of Asia, particularly China and India, in this respect. These include:

1. Growing numbers of co-development partnerships between domestic companies in India and China and their foreign counterparts for the purposes of joint discovery and/or drug development activities

2. Financing of innovation activities within emerging markets firms by large multinational pharmaceutical corporations in return for future development/marketing rights.

3. Emergence of a new and fast-growing crop of service-based businesses with a focus on providing sophisticated and cost-effective research, development, and manufacturing services to other, usually foreign, companies.[12]

4. Acquisition of domestic biopharmaceutical firms by foreign entities.[13]

5. Growing R&D presence of large pharmaceutical firms in China and India. Two of the largest commitments in this respect include a US$ 1.25 billion investment in by Novartis (Paris, France), announced in 2009, to build China's largest pharmaceutical R&D centre and an advanced technical R&D and manufacturing facility.[14] Most recently, Merck & Co. announced a five-year US$1.5 billion investment into a R&D facility in Beijing set to employ about 600 people.[15] This adds to the latter company's 3,000 person sales force in the country that has grown 90% in only three years.[16]

It is easy to view technological advancement in China and India as a competitive threat to incumbent innovator nations and firms. Indeed, in the generics pharmaceutical segment and the pharmaceutical ingredients markets Indian and Chinese firms have proven that they are formidable global competitors. **However, to consider the rising technological and innovation capacity only in competitive terms misses half the story – namely the considerable opportunities that these developments present for the Canadian industry and healthcare consumers.**

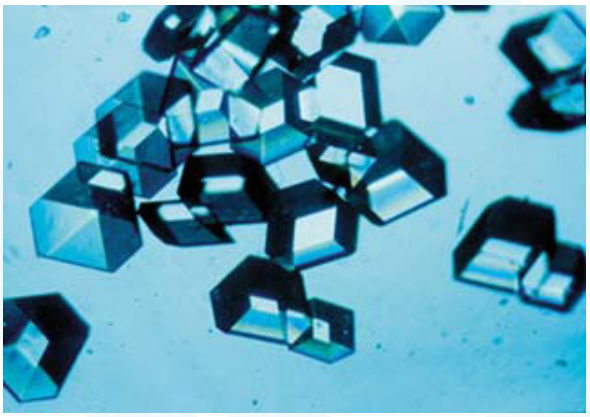

Photo Credit: NASA/Marshall

However, making the necessary adjustments to prosper from technological advancement in these emerging markets demands a different mindset. We no longer have the luxury, if we ever did, of internalizing the various components of an innovation system necessary to discover and develop high-tech products and blast them out into the world. This challenge is not limited to the time-consuming and resource-intensive biopharmaceutical innovations, but can increasingly be seen in other sectors such as in the information technology sector. The key question is will we make the necessary and timely adjustments to prosper from the rising innovative capacity in the emerging markets?

Emerging Innovation Opportunities for Canada

Innovation: Collaborative and Fragmented

Co-development and outsourcing are clear and decisive shifts in the way that medicinal innovations take place. This focus on distributed innovation is a function of the failure of previous approaches, which emphasized that very large and fully integrated firms were most suitable to innovate in new drugs. **Collaborative arrangements – that increasingly include companies in emerging markets - are now seen as a way to contain innovation costs, minimize investment risks and access new markets.** Innovative firms in emerging markets such as Hutchison Medipharma (Shanghai), Suven Life Sciences (Hyderabad), Glenmark, and Piramal Life Sciences (both in Mumbai) are early practitioners of this model and work with major pharmaceutical MNCs to discover and develop new therapies.

The emergence of a significant number of R&D service providers in China and India is also facilitating outsourcing of drug discovery and development activities to vendors in these markets. China's Wuxi Pharmatech and India's Advinus Therapeutics are among a growing crop of firms that cater primarily to foreign firms and provide services from early discovery to preclinical and clinical development stages. Depending on the type and nature of these activities, cost savings resulting from outsourcing can be in the 30-60% range, as compared to the US or Canada. This would suggest that Canadian biotech SMEs, with limited financial resources, could similarly benefit from similar engagements. However, there is a dearth of Canadian biotech companies that engage partners in China and India for joint innovation/co-development projects. This undoubtedly is related to the inherent challenges of operating in these markets and the real or perceived risks of IP infringement. Notwithstanding these factors, and given the size of biopharmaceutical industry in Canada, and the rising demand for technology and know-how in China and India, one would expect a greater level of linkages between Canada and these markets. In contrast, one sees involvement from US-based entrepreneurs in all areas of the sector in China and India. We need to ask ourselves 'are they seeing something we don't?' This question is particularly pertinent given that much of the growth in the global pharmaceutical sector now comes from the emerging markets.

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Collaborative product development with partners in these countries themselves not only has the potential to reduce development costs, but also to ensure that the end products are more suitable for the emerging markets themselves. A strategy used successfully, particularly by Indian Companies has been to innovate on price – sometimes called 'frugal innovation.' This approach has been used profitably to improve access to health products for locals. This objective has been accomplished in terms of both health products (e.g. Shantha Biotechnics' hepatitis-B vaccine and Biocon's Insulin)[17] and service delivery (e.g. the Aravind Eye Hospitals that last year treated over two million patients and conducted 300,000 surgeries at a very low cost relative to those in the developed world).[18] The key

point is that if we want to address emerging markets with our innovations we ought to innovate with the eventual consumer in mind from the outset. Innovating with those closest to market needs can be an effective strategy in this respect.

The Market for Technology; Growing and Largely Untapped

As indigenous industries in emerging markets transition to innovation, there is little doubt that they have a significant need, at least over the short-term, for new molecules, technologies and know-how. This is also true for some developed economies such as Taiwan, which is actively seeking to in-license new drug candidates in early clinical trials for further development in the country. Canadian biopharmaceutical SMEs are well positioned to meet some of the technology needs of Asian economies. Below are a few examples of Canadian companies that have successfully tapped the market for technology in China.

Welichem Biotech (Vancouver) established a partnership with Weihe Pharmaceutical (Yuxi, China) and Celestial Pharmaceuticals (Shenzhen, China), through which the company received $50M investment into Welichem. The companies set up a Joint Venture in China for drug discovery using Welichem's Technologies.

Calgary-based Symbiosis Genetics recently signed an agreement with China's Tasly Pharmaceuticals to sell its technology in return for 30% ownership in a joint venture to develop and commercialize a host of products globally. The companies disclosed that Tasly is to contribute all of the research, development and commercialization costs.[19]

Microbix Biosystems Inc. (Toronto) has set up a joint venture with Hunan Biomedical Park and the Hunan province to build a US$ 200M influenza vaccine manufacturing plant. Recently, Microbix Biosystems and Zydus Cadila, an India-based global pharmaceutical company, signed a Letter of Intent to market the thrombolytic drug, Urokinase, in the North American markets. The facility is targeted to have a capacity for 500 million doses of vaccines annually, making it the largest of its kind in Asia and third largest in the world. The plant, scheduled to be operational in 2013, is being designed usingMicrobis's VirumaxTM technology, which improves vaccine yield considerably. As part of the agreement, the Hunan province has also agreed to purchase up to 100 million doses of vaccines over seven years.[20]

Lastly, Montreal based ProMetic Life Sciences Inc. has had an ongoing partnership – revolving around the company's protein purification technologies – with the Wuhan Institute of Biologic Products (WIBP) and its parent company, China National Biotech Group (CNBG) for a number of years. According to their latest agreement, in addition to their manufacturing activities in China, the partners plan to establish a new facility to manufacture plasma-derived therapeutics in Laval, Quebec. "The net result for both parties is an accelerated and more cost effective route to commercialization", says Mr Laurin, CEO of Prometic, which provides an enabling platform for manufacturing of biopharmaceuticals.[21]

Photo Credit: Bmramon

Resource Flows: Bidirectional at Last

Another emerging trend – also observed by Prof. Halla Thorsteinsdóttir and her team[7] – is for capital and technology to flow from emerging and developing countries to what we typically think of as developed

markets. This trend is likely to grow significantly in the coming years as economic growth and increased innovation activities strengthen the financial and technological status of emerging market firms. Although this trend is much more pronounced in relation to the US and Europe, a couple of Canadian examples illustrate this point.

India's Piramal Healthcare (Mumbai) has made considerable investments in Canada. It owns a 120-person research and manufacturing facility in Aurora specializing in active pharmaceutical ingredients. In 2006 it invested US$ 6 million in Montreal's BioSyntech and in 2010 purchased its assets after the company declared bankruptcy. It continues to operate under the Piramal Healthcare brand. Piramal Life Sciences, an India-based subsidiary, and Dr. Reddy's Laboratories (Hyderabad) have conducted a number of clinical trials in Canada in recent years.

YM BioSciences of Toronto is conducting clinical trials for an anti-cancer molecule that originated in Cuba's Centre of Molecular Immunology. The drug, named Nimotuzumab, is already on the market in 20 countries including China and India, but is not yet approved in the Canada, US, Europe or Japan.

Recent analysis (unpublished) has identified over three hundreds vaccine and drug candidates within the pipelines of domestic firms in China and India. Roughly half of these are new-to-the-world type of innovations. Most of these are destined to be outsourced at later stages of development and/or will need to utilize resources of other firms to be commercialized. Canadian biopharmaceutical firms have the opportunity to stay on top of these emerging trends, and can benefit by in-licensing of promising technologies or assisting in their development.

Development Aid: Teach them Fishing

Canada has a long and proud history of contributing to international development. However, as the University of Toronto professors Peter A. Singer and Janice G. Stein have argued, our approach to development assistance has not kept pace with the changing economic realities in much of the developing world. They suggest that we should dedicate more of the Canadian development aid budget to help improve science, technology and innovation capacity in the developing world. Grand Challenges Canada (www.grandchallenges.ca) as an initiative that aims to advance health in the developing world by helping to remove specific critical barriers, is a first attempt at doing just that. However, it represents only a small portion of our development aid budget. There is much greater scope for initiatives that help to accelerate technological advancement in the developing world and enable domestic entrepreneurs to address more of their own challenges. **Successful development aid, like an effective vaccine, should aim to eradicate its own market. It is not clear that our present approaches are aligned this way.**

We could also leverage Canada's considerable experience in offering public healthcare insurance and services to help countries like China achieve their objectives of offering universal care to their citizens. Canadian experiences and social benefits of approach to health and healthcare remain a mode to the world and we should more actively tout its social and economic benefits in emerging markets with underdeveloped healthcare sectors.

Greater scientific and technological engagement with emerging markets and other developing nations is likely to have positive long-term benefits to Canada.

Innovations ultimately benefit everyone, and a larger pool of innovators in health could help contain healthcare costs. Canadian firms that provide hospital equipment and services could benefit from the rapid expansion of health services in China, India and other emerging markets. Lastly, in a report for the Canadian International Council[22] Catherine Côté highlights that bilateral relations with China can help safeguard medicinal supplies for Canadians as Chinese ventures begin to export products in much greater quantities.

Conclusion

China and India and a handful of the Asian countries are betting on biotechnology and pharmaceuticals as never before. Having made the choice to innovate in these closely related sectors, they remain in immediate need for much of what Canada has – knowledge, know-how, technology and how to deliver world-class healthcare. We also have a tremendous resource vis-à-vis our human Diaspora connections, which can facilitate relevant exchanges. We should think deeply and holistically about how we can leverage these and other advantages to become part of the growth story in Asia for years to come.

If we continue to think about marketing our technologies and intellectual property as merely "exporting of jobs," as some might argue, we will miss the boat. Canada has always generated many more ideas than it could ever develop and commercialize independently, and now is no different. If we accept that we are in a knowledge economy, where knowledge is, by definition, a key resource, then surely we need not only the capacity to process that resource, but to export those we cannot or choose not to process. We have little difficulty in recognizing the need for pipelines, shipping lines, or other transfer mechanisms for resources such as oil or other mining by-products. Few also argue that we should only export these when we have fully processed them to their 'end products,' be they purified gasoline or car tires. Yet, this logic seems to be at work when we think about knowledge. **There is considerable consensus that Canada is a resource-based economy. We should think of knowledge as one of these resources – to be discovered, processed, protected and traded.**

In the rapidly globalizing knowledge-intensive high-tech sectors innovative success will depend on the ability of nations to adapt scientifically, nationally, sectorally and globally all at the same time. We need to appreciate that while invention may be a local or national phenomenon, innovation is increasingly a global game. Our institutions need to adapt to the ideas of 'co-creation' and 'open innovation,'[23] where our markets, suppliers, collaborators and competitors may often be the same entities. To adopt 'open innovation' at a national level would mean that we protect and externalize those ideas that we are not developing and internalizing those that we can add value to. Presently, we do not have sufficiently coordinated mechanisms to implement such interventions in an efficient manner. To operate in the emerging global context, we need to:

1. Vigorously protect our intellectual property and facilitate its monetization at a global level

2. Extend our operational notion of technology transfer – usually thought of as university to industry transfer – by building competence in global knowledge and technology transfer

3. Support our researchers and companies (especially SMEs) to establish appropriate partnerships and linkages in emerging markets

4. Support Canadian entrepreneurs not only in seeking markets for products, but also the emerging markets for high-tech services and technologies

5. Be cognizant of opportunities for 'reverse' flows of knowledge and other resources, where the latter originate in emerging markets and other developing nations

To prosper amid this complexity demands a state that is at once both inward- and outward-looking. While globalization of knowledge and technology may be weakening certain levers that nation states have traditionally enjoyed, they are also creating new paths to prosperity. The capacity to explore opportunities in a timely and efficient manner and to find effective ways to take advantage of them requires a different set of competencies at the level of both states and

industries. The quest towards enhanced innovation capacity is particularly alive in Asia today. We should explore what it means for us and not be blindsided by its consequences.

A Recent report by the Canadian International Council entitled "Open Canada: A Global Positioning Strategy for a Networked Age" aptly observed: "Canada is top notch, particularly in medical sciences. But we are not leveraging this knowledge for national advantage". It went on to Say that: "all nations prosper from the spread of innovation but the first movers benefit disproportionately. Unfortunately, Canada is often a latecomer." When it comes to leveraging the burgeoning high-tech innovation capabilities in the emerging markets to our advantage – at least in the biopharmaceutical sector – we are not yet a latecomer. But we do not have much time.

Table 1: R&D Expenditures and Share of Global Scientific Publication for China, India and Select Other Countries.

Country	R&D Expenditure as a % of GDP[1]	Gross Domestic Expenditure on R&D (GERD) in Billions USD[1]	Share of Global Scientific Publications [Annual Growth Rate of Scientific Articles b/w 2000-2008][2]	Annual Growth Rate in Patenting (2000-2006)[2]
China	1.5 (2008)	102 (2007)	12%, 2008 [23.4%]	26.5%
India	0.80 (2007)	24.8 (2007)	2.3%, 2006 [4.7%]**	42%*
Brazil	1.10 (2007)	20.3 (2007)	1.6%, 2008 [12.2%]***	N/A
Canada	1.84 (2008)	24.0 (2007)	2.7%, 2008	3.9%
Germany	2.54 (2007)	72.2 (2007)	4%, 2008	5.7%
Japan	3.44 (2007)	148 (2007)	4.8%, 2008	4.5%
United States	2.82 (2008)	398 (2007)	16%, 2008	2.6%

Sources: [1] UNESCO Science Report 2010.
[2] OECD Science, Technology and Industry Outlook 2010.
* Estimate for India is for period 1997-2004.
** Estimate for India is for 1995-2005.
*** Estimate for Brazil is for 1998-2008

Table 2: Pharmaceutical Market Size and Growth Rates in China, India and Select Other Countries.

Country	Pharmaceutical Market Size, $ billions, 2010 (Projected Size in 2015)	CAGR for Pharmaceuticals (2006-2010)	CAGR Forecast for Pharmaceuticals (2010-2015)
China	25.7 (48.8)	17.3%	13.6%
India	14.1 (30.4)	16.6%	16.6%
Brazil	15.3 (34.4)	13.1%	17.6%
Canada	26.6 (30.2)	5.4%	2.6%
Germany	37.9 (41.5)	3.4%	1.8%
Japan	72.4 (102.7)	4.4%*	7.2%**
United States	292.8 (344.7)	2.9%	3.3%

Sources: DataMonitor 2010, Country-specific Pharmaceutical Industry Profile Reports.
CAGR stands for Cumulative Annual Growth Rate.
* Data for 2005-2009.
** Data for 2009-2014.

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[12] Companies adopting the R&D services model model – such as China's Wuxi Pharmatech and India's Advinus Therapeutics – typically serve foreign clients by focusing on discovery and development as well as contract manufacturing for proprietary health products
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[22] Catherine Côté (2010). Ensuring Canadians Safe Access to Pharmaceutical Products through Canada-China Cooperation. Canadian International Council (www.canadianinternationalcouncil.org).
[23] I am borrowing the term "open innovation" from Henry Chesbrough's book by the same title, premissed on the idea that firms can benefit by adopting external ideas that they can add value to and externalizing those ideas that they posses by cannot, or do not plan to develop. For discussion pertinent to the present article, the same concept is extended to apply to the nation state.
[24] Canadian International Council Report entitled "Open Canada: A Global Positioning Strategy for a Networked Age" (http://beta.images.theglobeandmail.com/archive/00690/Open_Canada__A_Glob_690863a.pdf)