Center for Global Development

Global Health Frontiers:
Expanding Access to Medicines to the Poor in Emerging Economies

by

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Center for Global Development

Independent Research and Practical Ideas for Global Prosperity

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Introduction

The emerging market countries of Brazil, Russia, India, China and South Africa (BRICS)—which are on track to become the world's largest economies—represent the greatest pharmaceutical market growth area today. Their individual income and wealth is growing at the fastest rates in the world, their middle classes are growing rapidly, and the individual and collective purchasing power of consumers is increasing daily.

While the global health community tends to focus on infectious diseases, the primary diseases that occur in emerging economies are the same as those in high-income countries—chronic diseases. Thus, the medicines, diagnostics and devices needed in emerging market countries overlap with products that major pharmaceutical companies have already developed or will develop. This means there is an opportunity to address major health issues in these countries and for pharmaceutical companies to expand the market for their products without having to invest in new research and development (R&D) programs.

These emerging markets, however, differ from traditional markets:

- Sales are high volume and low margin;
- Healthcare systems differ dramatically in structure from the traditional markets and from each other;
- Equity in access to healthcare is a more acute issue and a political imperative;
- Emerging market regulatory regimes are not well understood; and
- The situation is dynamic, as policies that define the operating environment change rapidly.

These factors require a different business model, one that must, for moral and business imperatives, take into account access to medicines across the economic spectrum.

Not only are opportunities in emerging market economies expanding, but growth in traditional pharmaceutical markets is slowing. The current business model, which focuses on a small number of high-income countries, is under pressure and of decreasing value to investors. While the greatest percentage of overall revenue of multinational pharmaceutical corporations still comes from traditional markets, much

of the future market opportunity will come from emerging markets under a different set of rules.

Despite the obvious health needs and the phenomenal growth of the pharmaceutical markets in the BRICS, there are many barriers to serving these markets: weak health systems, low per capita health expenditures, regulatory barriers, protectionist industrial policies, and the high price of new medicines relative to income. This means that a large percentage of the poor in these countries remain unable to access needed medicines.

As multinational pharmaceutical companies contemplate the future, and as new corporate players grow within the emerging economies, it is critical that public sector players work together, and with the pharmaceutical industry, to find creative solutions that increase access to medicines throughout the economic strata while respecting the business motivations that could fuel that access.

Pharmaceutical Companies Have Growing Opportunities in Emerging Market Countries

The new frontiers in pharmaceutical markets are the world's emerging economies. Economic development in these economies is growing at nearly double the rate of that in high-income countries. In addition, emerging market countries are home to a vast percentage of the world's population. Finally, the disease profiles and the medicines needed to treat individuals in these countries are similar to those seen in traditional pharmaceutical markets. As traditional pharmaceutical markets face continued economic slowing, emerging markets are an enticing, and largely unexplored, frontier.

The Economics

Economic predictions indicate that emerging economies will overtake the world's established economies within the next five to 40 years (Table 1) (Purushothaman & Wilson, 2003). Industries are contemplating these global changes and developing strategies that will allow them to survive and thrive in an economic system that differs drastically from today's. The rise of the emerging BRICS economies appears inevitable, but how these countries will rise, and how they will influence and change current business models, remains unknown.

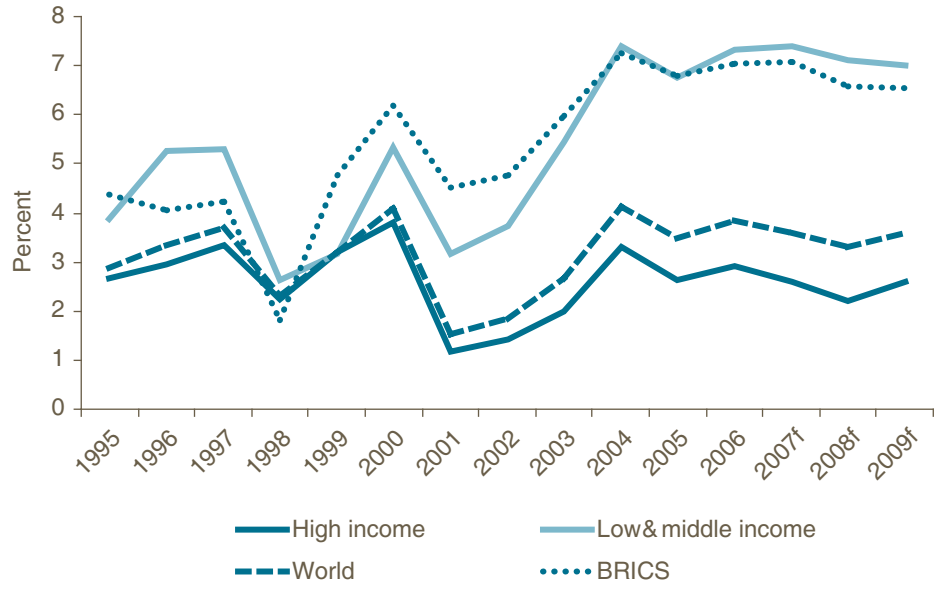
Although one BRICS country, South Africa, does not make the top-10 list by 2050, its growth is significant and its role on the African continent potential-

Table 1: Ranking of Economies by Size

GDP 2000	Projected GDP 2050
United States	China
Japan	United States
Germany	India
United Kingdom	Japan
France	Brazil
Italy	Russia
China	United Kingdom
Brazil	Germany
India	France
Russia	Italy

Sources: Purushothaman & Wilson, 2003; World Development Indicators, 2008.

Figure 1: Annual GDP Growth (percent)



Source: World Development Indicators, 2008.

ly important for access to medicines in this region. Projections indicate South Africa will grow at a rate of 3.5 percent and have a US$1.1 trillion economy by 2050. Because of declining population growth rates, projections indicate its per capita income will be higher than those of China, Russia and Brazil by that time.

Economic growth in low- and middle-income countries is robust and exceeds global trends. The greatest growth in GDP is occurring in low- and middle-income economies (Figure 1), which showed growth at 7.5 percent in 2006, 7.4 percent in 2007 and projections of 7 percent or more in 2008 and 2009. This compares to a world GDP growth rate of 3.9 percent in 2006 and 3.6 percent in 2007. The combined BRICS GDP growth rate was 6 percent in 2006. The past decade shows clear historical trends and indicates that these trends will continue (World Development Indicators, 2008) (The World Bank, 2008).

Per capita income tells the story of individual wealth. In emerging markets, per capita income is rising, as poverty declines and large numbers of people enter the middle and upper classes.

Projections for the next 10 years suggest that developing countries will achieve per capita income gains of 3.9 percent and perhaps as much as 3.4 percent in the following decade: more than double that projected for high-income countries. GDP per capita growth in BRICS countries from 1995 to 2000 was 2.9 percent and rose to 5.2 percent for the period between 2001 and 2006. Thus, not only are the overall sizes of the BRICS economies growing, but individual wealth is also increasing rapidly.

In South Africa, the black middle class grew by 30 percent in just over a year, with their numbers increasing

from two million to 2.6 million and their collective spending power rising from R130 billion to R180 billion (SouthAfrica.info, 2007). Mckinsey & Company predict India's middle class will grow from 50 million today to 583 million by 2025, and overall income levels will almost triple (Ablett, et al., 2007). By 2025, China will be one of the largest consumer markets in the world, spending about US$2.5 trillion annually (Farrell, Gersch, & Stephenson, 2006).

The number of people living in poverty worldwide is declining, as the growth in per capita income has also benefited the poorest individuals. The global measure of extreme poverty is those living on less than one dollar per day. In 2001, an estimated 1.1 billion people lived on less than one dollar per day: almost 400 million fewer people than did in the previous 20 years.

The People

The vast majority of the world's population (83 percent) lives in low- and middle-income countries, and projections indicate this percentage will increase to 86 percent by 2015. In 2005, the global population was 6.5 billion people, of which one billion lived in high-income countries, 3.1 billion lived in middle-income countries and 2.1 billion lived in low-income countries. The BRICS population alone totaled 2.8 billion or 43 percent of the total population in 2005 (World Development Indicators, 2008).

The world's population is also aging rapidly. By 2020, 9.4 percent of the world's population will be 65 years old or older, compared with 7.3 percent in 2005. This is significant, because disease patterns differ in older populations, and older individuals consume more medicines.

In BRICS countries, there are about 44.5 million live births each year, with 88 percent occurring in China and India. Children are the primary recipients of vaccines in developing countries.

The Disease Profile

Even though much of the focus of the "Access to Medicines" movement has been on the biggest infectious disease killers—HIV/AIDS, tuberculosis (TB) and malaria –, chronic diseases are the greatest cause of morbidity and mortality worldwide, leading to 60 percent of all deaths. About 80 percent of these deaths occur in low- and middle-income countries (World Health Organization, 2005). For example, cardiovascular disease (CVD) in such countries killed over twice as many people in 2001 as did HIV/AIDS, malaria and TB combined. The principal chronic diseases are cardiovascular disease (17 million deaths), cancer (7 million deaths), chronic respiratory disease (4 million deaths) and diabetes (1 million deaths).

Therefore, there is substantial overlap in emerging market country diseases and the medicines that pharmaceutical companies already develop for, and sell in, high-income countries. Hence, the access question for pharmaceuticals that could meet significant health needs might have more to do with scale and pricing than with providing new incentives for R&D investments.

The overall patterns of disease differ somewhat by country economic status (Table 2). The greatest similarities occur with middle- and high-income

Table 2: Top Causes of Death by Income Level

Disease Rank	World	High-Income GNI per capita>$11,116	Middle-Income $905<GNI per capita<$11,116	Low-Income GNI per capita<$905
1	Ischemic heart disease	Ischemic heart disease	Cerebrovascular disease	Ischemic heart disease
2	Cerebrovascular disease	Cerebrovascular disease	Ischemic heart disease	***HIV/AIDS***
3	***HIV/AIDS***	Lung cancer	Chronic obstructive pulmonary disease	Cerebrovascular disease
4	Chronic obstructive pulmonary disease	Diabetes	***HIV/AIDS***	Chronic obstructive pulmonary disease
5	***Lower respiratory infections***	Chronic obstructive pulmonary disease	Lung cancer	***Lower respiratory infections***
6	Lung cancer	***Lower respiratory infections***	Diabetes	Perinatal conditions
7	Diabetes	Alzheimer Disease	Stomach cancer	Road traffic accidents
8	Road traffic accidents	Colon cancer	Hypertensive heart disease	***Diarrheal diseases***
9	Perinatal conditions	Stomach cancer	Road traffic accidents	Diabetes
10	Stomach	Prostate cancer	Liver cancer	***Malaria***

Bold italic text = Infectious Disease.

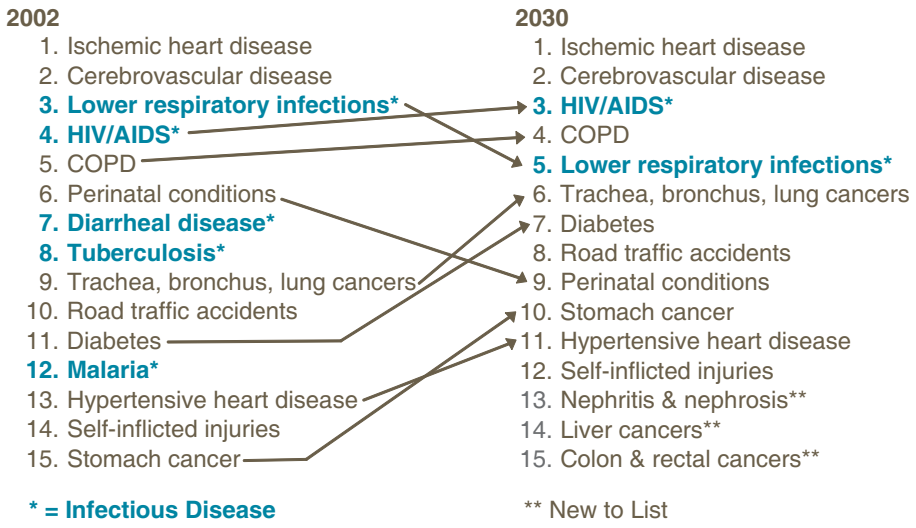
Sources: Mathers & Loncar, 2006.

countries, as chronic diseases compose the vast majority of the top causes of death. In low-income countries, both infectious and chronic diseases cause significant morbidity and mortality.

The correlation between chronic diseases and country economic levels could support the notion that these are diseases of the affluent and, thus, a less worthy target for global health and development assistance. It is clear that low- and middle-income countries suffer significantly from chronic diseases, but it is less clear if the disease distribution falls evenly on different economic strata. Available data focus primarily on risk factors rather than actual disease. There is clear evidence in low-income countries that smoking rates are higher among the poor, and while limited data suggest that diabetes and angina predominate among the rich, the greater likelihood of the rich to seek a diagnosis might skew these numbers. In high-income countries, the data show that the poor carry a higher chronic disease burden than the rich (Mackenbach, 2005). Thus chronic diseases do not disproportionately affect the poor more than the rich but even an equal distribution still results in a heavy burden of chronic diseases among the poor.

Current predictions indicate that chronic diseases will increase over the next 10 years and account for 76 percent of all deaths (Figure 2). A few factors play a substantial role in this phenomenon: rapid relative growth in the population of older individuals (who manifest a higher proportion of chronic diseases); urbanization; and important

Figure 2: Disease Burden—Present and Future Projections



Source: Mathers & Loncar, 2006.

lifestyle changes. The growing health problems in emerging economies will increasingly mirror those of high-income economies for which most pharmaceuticals are developed.

Expanding Pharmaceutical Marketplace in BRICS Countries

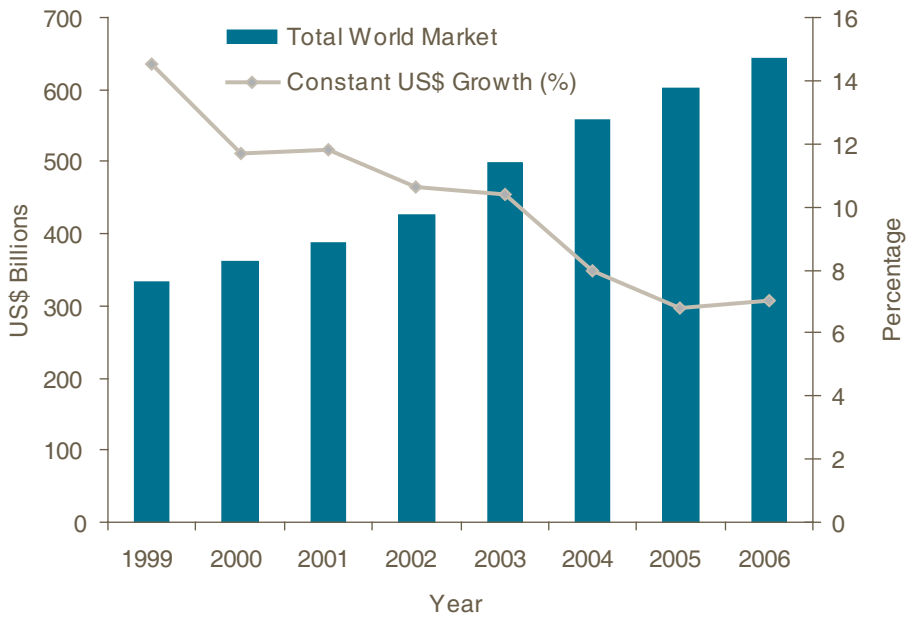
In sharp contrast to the declining growth rates seen in the global pharmaceutical market (Figure 3), emerging markets and middle-income countries saw substantial growth rates in the industry in 2006.

While the U.S. accounted for 50 percent of global market growth in 2006, 27 percent also came from countries with a gross national income (GNI) of less than $20,000 per capita (PPP).This is in contrast to 2001, when low-income countries accounted for only 13 percent of total growth.

The BRICS countries had an average growth rate in the pharmaceutical sector of over 10 percent in 2007, compared to a world growth rate of 7 percent. The Russian pharmaceutical market more than tripled between 2000 and 2004 and is now one of the fastest growing in Europe, with a total market size of US$5.8 billion in 2006. Pharmaceutical growth in China was 12.3 percent in 2006 and is expected to rise to 13–14 percent in 2007. Brazil saw growth of 11.3 percent in 2006, and in South Africa current growth is about 11 percent.

Predictions indicate the Indian market will triple to US$20 billion by 2015 and become one of the world's top 10 pharmaceutical markets. This growth trend is expected to continue in Russia, as well, with sales forecast to increase by 10 percent per year through at least 2010 (IMS Health, 2006). Contrasting with the high expected growth

Figure 3: Global Pharmaceutical Market Trends



Sources: IMS Health, 2006.

rates in the BRICS, the total projected world sales growth in 2008 is only 4 to 5 percent. The highest growth levels in the pharmaceutical marketplace today occur in emerging markets, as growth in traditional markets simultaneously slows. Overall, revenues continue to climb, but of considerable concern to investors is the fact that the overall growth rate of the pharmaceutical industry continues its decreasing multi-year trend.

The highest revenue drug classes are for chronic diseases, including cardiovascular disease, cancer and diabetes. In 2006, the largest revenue therapy group was one that included lipid–lowering agents, which increased 7.5 percent to US$35.2 billion. The oncology market grew 20.5 percent to US$34.6 billion, and projections indicate that growth in this market will range from 17 to 20 percent between 2005 and 2010. For anti-diabetic medications, sales increased 13.1 percent to US$21.2 billion, and according to current estimates, this market will grow at a compound annual rate of 7–10 percent, reaching US$25 to US$29 billion by 2010 (IMS Health, 2006).

Both current and potential commercial returns drive investments in R&D by pharmaceutical companies. As a result, these profits roughly correlate with the leading causes of morbidity and mortality in high-income countries. As discussed above, the most burdensome diseases in high-income countries are also the primary causes of morbidity and mortality in emerging markets, resulting in an epidemiological overlap and a parallel need for pharmaceuticals.

There is considerable room for additional growth if companies pursue emerging markets seriously. For example, only 5 percent of sales of lipid-lowering agents were to the many countries that constitute the "Rest of World" (ROW) category, beyond the primary, rich-world markets. Only 11 percent of sales revenue from anti-diabetic medications comes from ROW countries. Emerging economies are a largely untapped resource that can reinvigorate the market for drugs and vaccines originally developed for high-income countries.

Access to Medicines by the Poor in Emerging Economies is Inadequate and there are Many Barriers to Ensuring Expanded Access

Not all members of the world's population have equally enjoyed gains in economic development and improvements in life expectancy; there remains an appalling difference in health outcomes between wealthier and poorer countries. In 2005, a person born in a high-income country could expect to live to the age of 80, while a person born into a least developed country only 52. BRICS countries have a life expectancy at birth of 63 years (68 years without South Africa) (World Development Indicators, 2008). Therefore, the average person in a developing country lives only 65 percent of his or her potential life span.

There are numerous reasons for life expectancy disparities, and access to lifesaving medicines is certainly an important one. WHO estimates that nearly one-third of the world's poor lack access to needed medicines, and in parts of Asia and Africa, that number is as high as nearly one-half. The current global trends are positive, as the proportion of people without access to essential medicines fell from a little less than one-half to around one-third between 1975 and 1999. However, when population growth is taken into account, the total number of people without access remained the same: approximately 1.7 billion. Improving access to essential medicines and vaccines could save an estimated 10.5 million lives every year.

If one only reads media reports, it would be easy to believe that the only barrier to access is the price of the medicine or vaccine. The actual picture is much more complex, with multiple barriers contributing to the lack of access and even multiple sources compounding the final price. Barriers to access include:

- Lack of finances;
- Weak health systems that cannot support the delivery of medicines and healthcare;
- Regulatory systems that are time-consuming, opaque and rapidly changing;
- Industrial policies that are at odds with health outcomes; and
- High prices of drugs and vaccines relative to income

Despite the opportunities that growth in emerging market countries might present, multiple barriers prevent access to medicines, and these access barriers disproportionately affect the poorest in those societies. This is a dynamic situation, as other forces lessen barriers to access as well. For example, the drive of Indian and Chinese manufacturers to export to high-income countries is strengthening intellectual property protection and regulatory law and practice. Thus, some significant historical barriers could shift dramatically as the emerging market countries engage more intensively in the global marketplace.

Health Systems

While the public and private sectors can choose to provide healthcare, the government sets the policy context and the operating environment. Governance in many low- and middle-income countries lags behind that of high-income countries, affecting everything from the policy environment to the number of local clinics that are open, staffed and stocked. Governance that is weak, unpredictable or unreliable can lead to: a dearth of appropriate policies for the rational use of medicines; delays in medicine purchase and acquisition, resulting from inadequate knowledge or excessive bureaucracy; and corruption in the purchasing and distribution of drugs, adding to the cost and reducing the overall health benefits of needed medicines. China and Russia are extreme examples of healthcare systems in transition: They are both moving from a centralized, planned system to a decentralized, market-driven system. India, Brazil and South Africa are more moderate examples but also have decentralization and marketization as two of their largest health sector reform issues. A driving concern in all of these transition economies is equity, as inequity in health is growing at a faster rate than the improvement in overall health outcomes. Tensions around equity play out most dramatically in debates about the price of medicines.

Government spending on health is rising in the BRICS countries, but not nearly fast enough to cover the large populations. Each of the countries is planning to implement, or is implementing, both private and social health insurance schemes. These schemes are not running smoothly in any of the BRICS countries, and a huge percentage of the populations are either not covered with insurance or are without the finances to pay out-of-pocket (with or without insurance).

Until the last five years, when there has been an injection of government health funding, the health systems of the BRICS countries were strained under insufficient financing and poor delivery systems for decades. In China and India, between the late 1980's and 2002–03, government spending on health as a proportion of total health spending decreased from nearly 30 percent to just over 15 percent (Ministry of Health, China Health Statistical Yearbook); (Karan, Mahal,& Selvaraj).

In China, the fall in government subsidies for public health facilities, coupled with the conscious desire to keep healthcare affordable, led the government to set prices for basic healthcare below cost. For the facilities to remain profitable, they charged high prices on diagnostic services and 15 percent

profit margins for drugs. These policies created greatly skewed incentives for facilities that then had to obtain 90 percent of their budget from profit-making activities such as drug sales (Yip & Mahal, 2008).

In contrast, the Indian government has heavily subsidized public facilities, in recent years, to provide low-cost services to the poor, while enacting minimal regulation to an ever-increasing private health sector. In an unregulated private sector, market failures run rampant, where medical professionals can engage in "commission-based referrals to diagnostic centers and adoption of high end medical technologies," the costs of which are all passed on to the consumer. This has led to poor quality, lack of access to drugs and high levels of absenteeism in the public sector, thereby thrusting patients into the private sector to be victims of excessive healthcare costs. (Yip & Mahal, 2008).

While China and India each set out to enact policies to increase access to healthcare for the poor, these new schemes have not yet brought about the desired improvements. Incentives in the delivery systems have become misaligned, government funding is not going where it needs to and out-of pocket expenditures have skyrocketed, especially among the poor, rural population, plunging more and more below the poverty line and without access to needed medicines (Yip & Mahal, 2008). While the BRICS economies steadily converge on the high-income countries in terms of absolute market size, their governance and policy environments must also mature, in kind, if they wish to see the fruits of their growth reflected in increased access to medicines for all and better health outcomes.

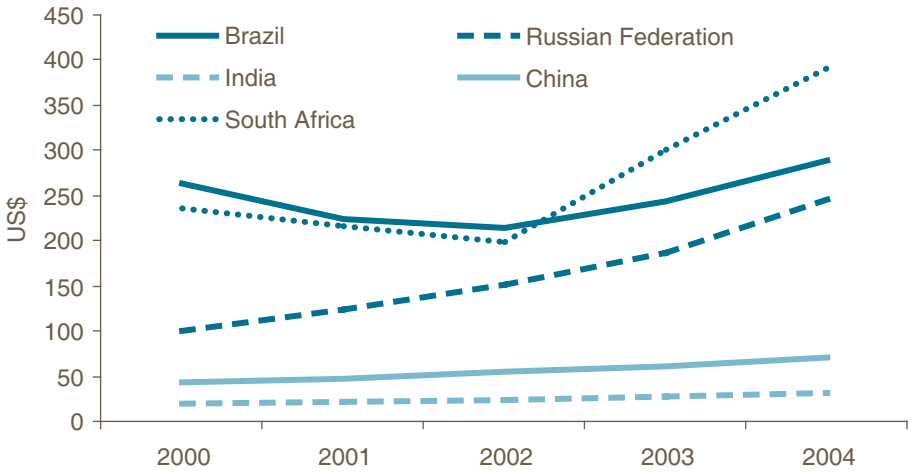
The Finances

Experts predict that emerging market countries will constitute the world's largest economies in the coming years; however, the structure of wealth will look very different from that of today's high-income countries. Currently, wealth tends to be concentrated in a small number of high-income individuals coexisting with massive numbers of poor. The middle class is growing, but the per capita income of high-income countries is more than 10 times that found in BRICS countries. Because of low population growth rates, projections indicate that per capita income levels in Russia and South Africa will increase in line with today's high-income countries. Brazil, China and India, on the other hand, will continue to have much lower per capita incomes, even as their economies grow.

Spending on health is increasing in low- and middle-income countries but remains far lower than the spending in high-income countries. Per capita health expenditure in 2005 was US$3,727 for high-income countries, US$141 for middle-income countries, and US$24 for low-income countries. From 2000 to 2004, average per capita health spending in BRICS countries increased by 55 percent to US$205. Thus, high-income countries spend 18 times more on health per person than BRICS countries. Figure 4 details these trends by individual BRICS countries.

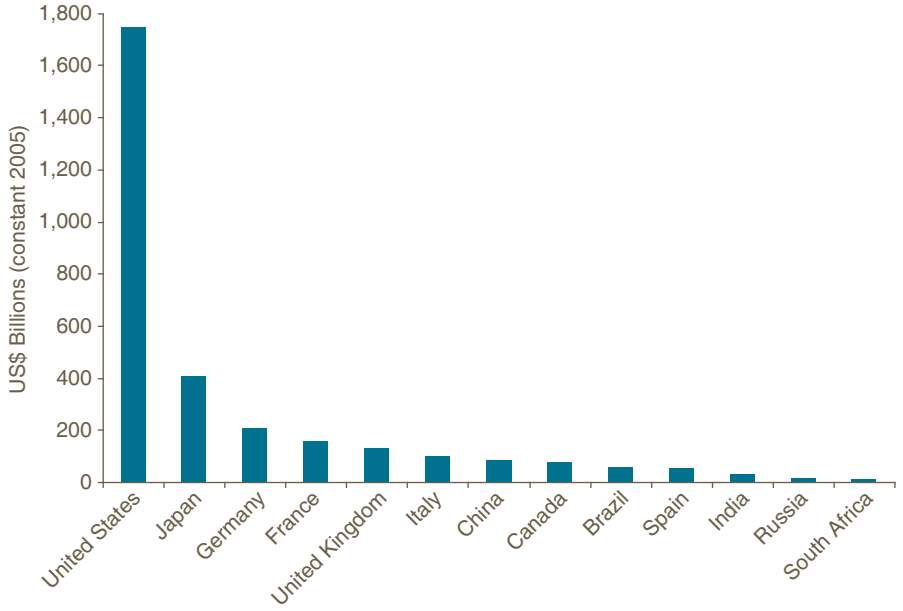
This disparity in per capita spending translates to an enormous imbalance in overall dollar amounts spent on healthcare. Figure 5 shows the 2005 total health expenditure of selected high-income and BRICS countries. While emerging market countries are

Figure 4: BRICS Per Capita Health Expenditure (2000–2004)



Sources: World Development Indicators, 2008.

Figure 5: 2005 Total Healthcare Expenditure by Country



Sources: World Development Indicators, 2008.

experiencing high economic growth rates, both the overall and per capita health expenditures remain a fraction of that of high-income countries.

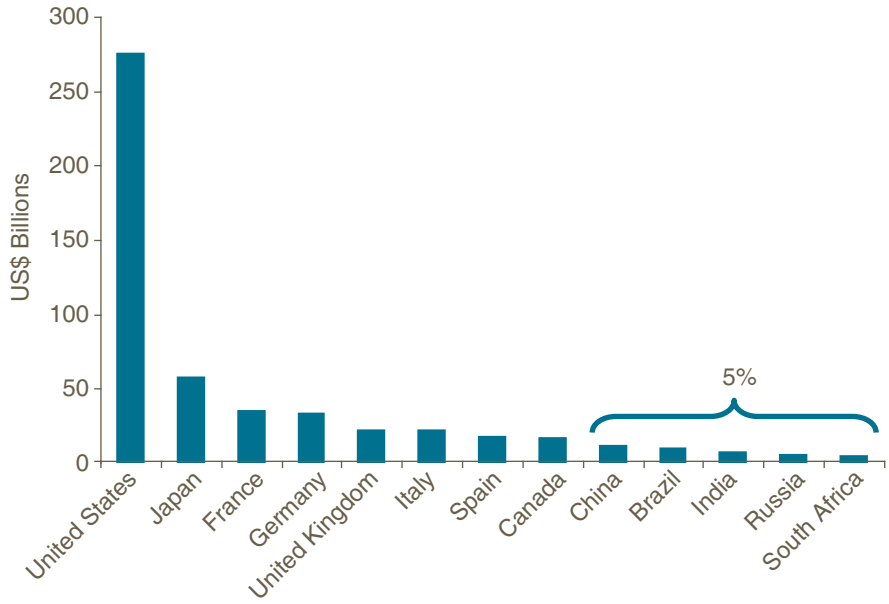
These spending patterns play out in the pharmaceutical marketplace as well, where high growth levels occur in emerging market countries, but high-income countries still dominate in terms of revenue (Figure 6). The U.S. alone accounts for almost 43 percent of the total market, while BRICS countries together accounted for only 5 percent of sales in 2006.

Although economic and pharmaceutical sales growth is dramatically higher in emerging market countries than in high-income countries, the amount of spending on healthcare and pharmaceuticals is dramatically lower. Thus, any actions that threaten traditional pharmaceutical markets will be of substantial concern to companies and to their investors, as revenues from emerging markets are not at the level to replace that lost value in the near term.

Regulatory Systems

Medicines registration is the process by which a national or regional regulatory authority approves the use of a medicine in a particular country, having considered evidence of the medicine's safety, quality and efficacy. In addition, regulation includes the ongoing assessment and inspection of the entire pharmaceutical supply chain—manufacturers, importers, exporters, wholesalers, distributors and final sellers –, maintenance of a register of approved products and post-marketing surveillance (including random quality checks and pharmacovigilance systems), control over the promotion and advertising of medicines and the provision of medicines information. There is a view that

Figure 6: 2006 Pharmaceutical Sales by Country



Sources: IMS Health, 2006.

issues related to the rational pricing of medicines and considerations of cost-effectiveness fall in the purview of the regulatory agency, but most see these considerations within the domain of health technology assessment (HTA) organizations.

The regulatory systems in most low- and middle-income countries are under-resourced and poorly equipped to assess increasingly complex data. The expertise necessary to regulate new chemical entities and complex biological products has rested almost entirely with large, experienced regulatory bodies in high-income countries. Many developing countries have relied on these approvals for their own internal processes, especially for new chemical or biological entities. Paradoxically, the regulatory burden is higher in developing countries than in OECD countries (Organization for Economic Co-operation and Development) (UK Department for International Development, 2006) (The World Bank, 2008).

The WHO has led a very successful effort to set international regulatory standards and processes, but each country develops and implements its own regulatory laws and practices from its own needs and experiences. The weakness of the international harmonization effort is that the agreements are non-binding, and many countries still either use their own standards or simply implement harmonized standards in different ways. The regulatory requirements are often unpredictable, as government regulations can change mid-process, making the process for registering drugs and vaccines in nearly 200 countries an expensive and daunting task for any company.

The regulatory situation in BRICS countries is highly dynamic. The desire of India and China to export medicines to high-income countries is driving much of the change; both countries have been upgrading their regulatory systems. In addition, the higher quality producers are applying pressure on the low quality producers to enhance the image of their products.

For some time, many industry experts have questioned the additional value of multiple regulatory reviews. The costs are considerable, and significant delays can occur in approvals at the country level. The U.S. Food and Drug Administration (FDA) has approved at least one new HIV drug that then took 18 months in the registration process in South Africa. There have been initial efforts to form regional regulatory bodies, but these initiatives have not yet reached fruition. The knowledge of how to improve the regulatory process is there, but the political will to change the situation appears weak.

Pricing

Among the many barriers that prevent access to medicines by the poor, price is the most discussed and the one for which the most theories flourish. Affordability is indeed a crucial determinant of access in developing countries, where medicines can account for 60 to 90 percent of household health expenditures (UK Department for International Development, 2006).

Taken together, personal finances in emerging economies and the price of pharmaceuticals can be a large barrier to access. If required to pay the same prices as people in high-income

countries, individuals in emerging markets and poorer countries would have to spend a much higher percentage of their income on medicines. The price of medicines to the end purchaser has multiple components. Even when pharmaceutical companies sell medicines at reduced prices to low- and middle-income countries, the price to the consumer is often much higher because of taxes and distribution costs. Many developing countries tax a wide variety of essential medical products, and tariffs can run high: 14 percent in South Africa, 16 percent in India, 18.3 percent in Morocco and more than 50 percent in Iran. One study found that these in-country additions routinely inflated the average cost of medicines and medical equipment by more than 20 percent (Bate, Tren & Urbach, 2006). Another study found that many countries, 39 percent, do not levy any tariffs on finished pharmaceutical products, forty-six percent have tariffs between 0 percent and 10 percent, and 13 percent of countries have tariff rates between 10.1–20 percent, the majority of which are in the lower-middle income and upper-middle income bracket. One percent of countries in the study imposed tariff rates of higher than 20 percent on finished products; India and the Islamic Republic of Iran (Laing and Olcay, 2005).

Tiered (or differential) pricing involves charging variable prices for the same medicines to different classes of buyers; in the access to medicines context, this usually means charging lower prices to the poorest countries than are charged to richer countries (Kaplan & Laing, 2005). The concept is to make medicines affordable to the poor while still allowing manufacturers to make a profit and to continue investing in the development of new drugs and vaccines. Tiered pricing has worked very well in the vaccine community for at least 20 years; the vaccine prices charged by the WHO and UNICEF's basic Expanded Programme on Immunizations (EPI) to developing countries are less than one-tenth of the prices in high-income countries.

Tiered pricing becomes a more difficult concept in the context of emerging markets: a small but growing number of elites can pay high prices for medicines; an increasing number of middle class individuals can pay some, with high out-of-pocket healthcare costs squeezing them; and massive numbers of poor can only afford drastically reduced prices. There is considerable interest in how to tier prices *within* countries, but there are few examples of this in practice. Novartis has developed three tiers for its anti-malaria drug, Coartem: it sells one version in Europe aimed at the traveler's market; it sells the same branded product to upscale urban pharmacies and private physicians in disease endemic countries; and it sells the product at no-profit prices to the governments of disease endemic countries for use in the public sector. Thus, Novartis is pursuing a dual-brand and triple-pricing structure for Coartem.

Industrial Policies

At the national level, industrial policies to stimulate economic development do not often align with health policies. As both health and economic development are critical to developing coun-

tries, it is understandable that countries would evaluate investments in pharmaceutical manufacturing using different criteria than the global health sector might.

To avoid dependency on the supply and pricing of imported medicines, many countries pursue self-sufficiency in the manufacture and sale of needed health products. Not surprisingly, their procurement policies and practices often favor local producers. A review of the substantial body of evidence on local manufacturing suggests that, many times, this approach results in products that are more expensive than those available for purchase outside the country (Kaplan & Laing, 2005); (Rey, 2008).

India has never introduced a new vaccine into use unless there were local producers who could supply the market. Brazil, meanwhile, has invoked compulsory licensing for several products, resulting in Brazilian generics companies manufacturing and selling the products. Article 68 of Brazilian law, allows the compulsory licensing of any product without needing the "public health emergency" that international patent and trade law calls for (Rey, 2008). While the intent of this effort was to obtain lower prices on medicines to serve a broader population, many perceive another aim: to build the pharmaceutical industry within Brazil.

Local production is also unlikely to bring countries access to R&D innovations in the shorter-term. High-income countries are the greatest source of higher-tech innovations (The World Bank, 2008); (SustainAbility, 2007). The innovation gap between high-income and developing countries is enormous, although growth is faster in the latter. Nevertheless, high quality, large-scale production of vaccines and medicines in BRICS countries is already a reality, and several of these emerging market manufacturers are investing heavily in R&D and expect to bring novel medicines to the market. National industrial policies might ensure preferential procurement of these products.

A New Business Model and Paradigm are Needed to Allow Companies to Operate in Emerging Markets with Acceptable Levels of Risk and in Ways that Enable Expanded Access to Medicines

Pharmaceutical companies still make substantial profits with the current business models that predominantly focus on sales in high-income markets; however, emerging pressures on these models suggest that they might not be sustainable. Growth trends are in a decade-long decline; much of the current revenue will be lost as patents expire; there are fewer blockbuster products to replace lost revenues; and growth in healthcare spending, as a percent of GDP, is causing governments and payers to put pricing pressures on new medicines.

Institutional investors in the pharmaceutical industry—concerned with the prospects for long-term value—commissioned the PharmaFutures project, conducted by the London-based consultancy, SustainAbility. The resulting report, along with numerous others, points to the challenges in sustaining the value of companies operating in the current marketplace (SustainAbility, 2007; IMS Health, 2006; PriceWaterhouseCoopers, 2007).

The characteristics of emerging markets call for a different business model than that previously pursued by pharmaceutical companies as the size of the pharmaceutical markets in emerging economies is still a fraction of that of high-income countries, the per capita income cannot support high prices, and the healthcare systems differ dramatically.

Companies face a dilemma when determining where to focus their primary efforts. Will companies try to eke out profits through a combination of cost cutting and a move toward high-priced specialty products? Will they seek new opportunities in emerging markets, with all of the inherent risks of that dynamic environment? Most large pharmaceutical companies are already pursuing both approaches, but the dominant focus remains on the traditional markets.

The road between the dominant business model of today—and one that will allow companies of the future to thrive—will likely be bumpy. The access-to-medicines question can seem an annoying intrusion into the corporate strategies of large companies; however, as posited here, it is a critical component of the corporate strategy of the future.

Current Business Model

Just 10 companies (all U.S.- or European-based) account for nearly half of global sales. The 10 companies in Table 3 account for US$282.1 billion in sales, which is 46.4 percent of the market. Companies outside the top 20 global firms each command less than 1 percent of the market.

Pharmaceutical companies employ different business models. At one end of the spectrum are large, "integrated," transnational corporations with the capacity to develop new molecular entities (originator products) and to manufacture, market and distribute medicines to most parts of the globe. At the other end are local producers who manufacture and distribute generic versions of drugs or traditional medicines. Situated in between is a wide range of companies differing in size, pharmaceutical products (originator and generic), and manufacturing and marketing techniques.

The dominant business model relies on developing "blockbuster" products that result in sales of greater than US$1 billion per year. The top 100 blockbuster drugs generated sales of US$232.2 billion in 2006, accounting for 36 percent of the total pharmaceutical market. Pfizer's Lipitor is the top-selling drug, with sales of US$13.6 billion in 2006. The number of blockbusters continues to grow; there were 44 in 2000 and 105 in 2006. However, the concern about continued reliance on blockbusters is that the pharmaceutical industry spends more on R&D than ever before and yet produces fewer and fewer new molecules (IMS Health, 2007).

Medicines for primary care have comprised the majority of the market share. A recent trend is the rise of specialty products. Primarily prescribed or influenced by specialty physicians,

Table 3: World's Top Pharmaceutical Companies by Market Cap

	Top Ten Companies: Total Sales		
	US$ Billion	% Global Sales	% Change from 2005
Pfizer	46.1	7.6	–.07
GlaxoSmithKline	37.0	6.1	5.5
Novartis	31.6	5.2	6.1
Sanofi-Aventis	31.1	5.1	1.4
Johnson & Johnson	27.3	4.5	1.2
AstraZeneca	26.7	4.4	11.2
Merck	25.0	4.1	4.9
Roche	23.5	3.9	16.1
Abbott	17.6	2.9	6.4
Amgen	16.1	2.7	20.6
Total	**282.1**	**46.4**	**5.7**

Source: IMS Health, 2007.

these products comprised 25 percent of the 44 blockbuster products in 2000 and 49 percent of the 105 blockbuster products in 2006. They contributed about 35 percent to growth in 2000, and 65 percent in 2006 (IMS Health, 2007).

The combined factors of more strict regulatory requirements for safety, the pressure to decrease R&D costs and the need to produce health outcomes sufficient to justify medicine expenditures are driving the growth of specialty products. Genomics allow companies to develop products that can more tightly target the mechanism of disease. It can also enable the identification of a patient population that is most likely to benefit from the product, providing companies the opportunity to conduct smaller clinical trials and still generate trial data that demonstrate product superiority. These products could become "serial blockbusters," as manufacturers identify new indications in other population subsets.

Pressures on the Current Business Model

The dominant pharmaceutical business model employed by most multinationals is under pressure to change. For a decade, growth efforts have focused on corporate boards attempting to increase profits by restructuring R&D and cutting sales and marketing to squeeze additional profit from current operations. Factors internal and external to the industry make it challenging to be optimistic about the current business model.

The growth in healthcare spending is not sustainable economically; if it continues to rise, by 2020, the OECD countries (excluding the U.S.) will spend 16 percent of their GDP on healthcare and the U.S. 21 percent, equalingUS$10 trillion. Unless there is a change in pricing, in practice or a turn toward prevention, this growth will remain unsustainable (PriceWaterhouseCoopers, 2007).

Because the rise in costs has not necessarily paralleled a rise in health outcomes, countries are increasingly turning to Health Technology Assessment (HTA) organizations. HTA parties assess the benefit of a new health technology (product or procedure) in light of its costs and advise the payors on reimbursement decisions.

An example of this is the National Institute for Health and Clinical Excellence (NICE) in the UK, an independent organization responsible for providing national guidance on the promotion of good health and the prevention and treatment of ill health. In 2006, NICE issued guidance that clinicians should not use beta-blockers as an initial therapy for high blood pressure. Instead, the organization recommended that clinicians prescribe all new patients angiotensin-converting enzyme (ACE) inhibitor, a calcium channel blocker or a diuretic. As a result, prescriptions for beta-blockers fell by 50 percent in three months, while prescriptions for ACE inhibitors grew by 30 percent (IMS Health, 2007).

High-priced medicines have returned robust profits to the industry and have paid for innovation. Some countries have been willing to pay higher prices for drugs and vaccines to ensure early access to innovation. The countries that contribute the highest revenue to the global pharmaceutical marketplace for branded products, however, have all implemented, or are considering implementing, cost con-

tainment measures such as NICE. With the huge growth in healthcare costs, high-income countries may no longer be willing to support drug and vaccine innovation through higher prices.

The move toward specialty products—and away from primary care products—adds pressure to the healthcare system. Specialty medicines tend to drive up healthcare costs, because they do not prevent disease. There has been little incentive to focus on primary care products, and in fact, the companies who do have fared the worst financially. It is too early to tell what effects HTA will have on pharmaceutical companies, but it seems probable that the pendulum will (or should) swing toward a primary care focus. The pursuit of specialty products will likely continue, as they constitute many of the new drugs in the pipeline and are, in the short term, where the profits lie.

In addition to pricing pressures, analysts expect the current pipeline of drugs to lose significant value over the next few years due to patent expiration. In 2006, brands that had lost patent protection dropped 21.7 percent market share compared with growth of 14.4 percent for protected products (IMS Health, 2007). An estimated US$157 billion in sales will be lost due to patent expirations, and the leading pharmaceutical companies will lose between 14 and 41 percent of their existing revenues (PriceWaterhouseCoopers, 2007); (Harris Interactive, 2006).

Thus, the current business model is unlikely to remain sustainable over the longer term. Efforts to trim costs and develop more specialty products are unlikely to make enough of a difference, and investors are commissioning studies on the future of the pharmaceutical industry because of these concerns. The pharmaceutical companies form a very powerful lobby group, especially in the U.S. While rising healthcare costs have affected the economic wellbeing of the society, the system has not yet reached a painful enough point to mobilize significant reform efforts. Change seems inevitable, and while the timeframe for that change is entirely uncertain, the sheer size of the U.S. market ensures it will continue to be the primary shaper of pharmaceutical industry behavior.

The opportunities presented by emerging markets, when paired with the decline in traditional markets, make it clear that companies will need to change or adapt their business models.

Implications for Access to Medicines

The opportunities in emerging markets have clearly caught the attention of major pharmaceutical companies. However, much of the effort, to this point, has been an extension of the current business model and results in small inroads to serving the affluent in those societies.

The characteristics of emerging markets will call for different business models; a low-price, high-volume model will need to evolve in order to serve the much larger populations, and high prices will not be feasible given the lower per capita incomes. The critical issue of equity will make it very difficult for a company to be a major player in a country without finding a way to serve the entire population. Emerging market countries are also under pressure to increase health outcomes at a societal level, pointing more toward primary care than specialist care.

Health systems in emerging market countries are very different from those in traditional markets, and it will be important to invest in creative ways to package medicines within programs that help to build the overall health system.

Lastly, trend data all point toward the economic emergence of BRICS and other middle-income countries. Each country is struggling, and will continue to struggle, with the best ways to change its laws and policies to support this growth. The dynamic policy environment will demand flexibility among those that want to take part in that growth, as well as a considerable amount of local knowledge.

There are Threats to the Pharmaceutical Industry for Not Playing in Low- and Middle-Income National Markets

At a time when the pharmaceutical industry most needs to influence the political agenda on healthcare, it has one of the lowest trust ratings of any industry. A Harris poll ranked the pharmaceutical industry 13th out of 17 industries for honesty—behind life insurance companies and carmakers (Harris Interactive, 2006). The perception that the pharmaceutical industry is indifferent to pressing global health

needs, for which it has many solutions, further undermines trust.

The awareness of issues related to access to medicines has changed dramatically in the past several years, with the rise of funding agencies such as the Global Fund to Fight HIV/AIDS, TB and Malaria; the GAVI Fund; and the work of the Clinton Global Initiative on access to anti-retroviral medications. Thus, there is an expectation at the global, regional and national levels of public health that companies will find ways to make needed health products available to poor populations. This is especially true for companies with a presence in emerging markets, as the rise of compulsory licensing is both a punitive response to this frustration and a genuine threat to companies not wanting to lose market share to generics.

Foundations, academic groups and non-profit organizations have grown frustrated and more sophisticated. They now adopt access-to-medicines provisions, and work with, or around, pharmaceutical companies. Years ago, there were few non-pharmaceutical options, but the rise of larger U.S. and European biotech companies and quality innovators in emerging markets provide other viable solutions. For example, there are 100 Indian facilities approved by the U.S. FDA to carry out contract research and manufacturing. R&D spending among the top 10 Indian companies is 7 to 8 percent of topline sales, compared with 3 to 5 percent of the industry as a whole.

Local and regional players could have an advantage in emerging markets due to protective industrial policies, cost structures, local contacts and traditional knowledge. Competition is increasing. This could result in a bypass of the multinational pharmaceutical industry and an erosion of its position in emerging and, eventually, world markets.

There are Also Threats to the Pharmaceutical Industry for Playing in Low- And Middle-Income National Markets

The danger of price erosion in the primary pharmaceutical markets is a prime concern of companies when operating in lower paying markets. The business model needed to fully serve emerging markets, however, will continue to rely on price tiering. With mounting pricing pressures in traditional markets, companies have been reluctant to tier newly launched products dramatically, for fear of eroding prices in major markets. The increased transparency around pricing (e.g. MeTa project) makes it easier for countries to quickly identify what others are paying for medicines and to demand similar prices. A current example is that the Pan American Health Organization wants to pay the same prices for vaccines that the GAVI Alliance, which represents the world's poorest 72 countries, pays.

Another valid concern is that of parallel importation. This can occur when a product is sold in one market at a lower price, and then the buyer sells the lower-priced product in neighboring markets for a higher price. Alternatively, the product could leak out of the public system and be sold for higher profit in the private system. Either way, the result is an erosion of profits.

Another key concern is that an adverse event in populations with different genetics and historical disease profiles from traditional markets could

jeopardize the entire product. For a country to use a product, it must receive regulatory approval. Often, regulatory or policy approvals require local or regional data, requiring companies to conduct clinical trials in the local populations. For this reason, many companies test and launch products in emerging markets years after the primary launch.

There is also a reputational risk when playing in developing country markets. The needs of these countries are vast, and often, the expectation is that the contributions from one source will solve problems far beyond what any one company can manage. It is a peculiar reality that the public sector often saves its harshest criticism for those companies that are trying to solve the problem rather than for those who just choose not to play. Thus, for a company with a product that poor people need, it is challenging to wade into these markets without fearing a loss of control resulting from public pressure.

What is Happening Today that Will Affect Access to Medicines?

Several efforts are underway to improve access to medicines in the public and private sectors; they range from innovative to draconian and show that there is considerable room for new thinking.

Improved Health Infrastructures

Poorer countries have less developed healthcare systems and are able to reach fewer people with a smaller number of health services than higher income countries. Many options exist that could help improve health services, even in advance of rising economic development. The GAVI Alliance recognized this for vaccines and created a pool of funds for health system strengthening, which has resulted in improved immunization rates in many of the world's poorest countries.

The upward trend in healthcare financing in BRICS countries, combined with health sector reform and the introduction of insurance schemes, will, hopefully, improve the services available and allow expansion to the broader population.

Price Transparency and Price Controls

Many countries across the spectrum of economic development are experimenting with ways to control the prices of needed medicines. For example, Brazil enacted a government program in 1998 that requires bioequivalents to be available at prices no more than 60 percent of the originator brand. This effort, while it aimed to increase access to medicines, has failed in this objective, because most growth in generics tends to come from higher-income individuals substituting generics for previous brands rather than from increased access (IMS Health, 2007).

To improve the negotiating power of buyers, public sector groups have formed the MeTa project, which aims to increase the transparency of drug prices in many emerging and developing economies. The concept is that by having reference points for pricing, purchasers will have a greater advantage when negotiating lower prices from suppliers.

Voluntary and Compulsory Licensing

Brazil, Thailand and South Africa have led well-publicized efforts to ensure that patented medicines are broadly

available to all of their citizens. The approach has been to either threaten compulsory licensing to bring about price concessions from multinationals or to actually enforce it and clear the way for domestic firms to make and sell patented drugs more cheaply. In some cases, voluntary licensing has been the negotiated settlement. It frustrates policymakers in these countries to know that drugs that could meet critical health needs are available but not affordable; hence, many have resorted to punitive measures with a strong moral argument to back them. On the other side, companies are working to preserve a system that has rewarded their enormous and risky R&D investments with ample revenue.

Clear and Consistent Pricing Policies

In 2008, several companies announced pricing policies for emerging and developing economies. Gilead published its pricing policy for anti-retroviral medications on its web site (Gilead Sciences Inc., 2008). GlaxoSmithKline (GSK), meanwhile, announced a "no profit" policy on sales of certain drugs to the developing world and has also published its prices for anti-retroviral medications. Of particular interest are the GSK pricing policies in middle-income countries for products such as its diabetes drug, Avandia. GSK is tiering prices between countries, but also within countries, hoping to compensate for lower price sales through increased volume.

Harmonizing Regulatory and Procurement Requirements

ASEAN (Association of Southeast Asian Nations) countries are building a common platform for drug registration, good manufacturing practices (GMP), inspection and labeling. There are several group procurement schemes, such as the Gulf Cooperation Council, the Eastern Caribbean Drug Service and the Pan American Health Organization's revolving fund for vaccinations. These efforts aim to contain costs and streamline the buying process for industry.

Financing

Financing schemes to buy needed health products for the poor have blossomed in the past decade, raising billions of new dollars for this purpose. The Global Fund for HIV/AIDS, TB and malaria provides funds to countries for the purchase of drugs, bednets and other health products needed for these three diseases. The GAVI Alliance purchases new and underutilized vaccines for the world's poorest countries and provides funds for strengthening immunization programs and health systems. UNITAID is a fund to purchase medicines for HIV/AIDS, TB and malaria and to support important activities in the development and regulation of new drugs for those diseases. In this same vein, also under consideration are funding facilities to purchase malaria drugs, funding schemes to purchase TB drugs and a possible asthma drug facility.

Conclusion

There is an amazing opportunity for growth, with increased attention on emerging markets. Access to both healthcare and cost-effective, lifesaving medical products for the poor can be ensured, while simultaneously creating sustainable business models for pharmaceutical companies. This is a new frontier, and the global health community will need to shift away from the subsidy mindset that currently dominates the field toward a cooperative, working relationship with industry, as they pursue hardcore, corporate strategies aimed at revenue growth.

The focus of the global health sector is on improving the health of the poor through the equitable provision of care and needed products. It is well documented, however, that massive numbers of the poor have access to neither. Access to medicines has been a difficult issue that, for the past decade, has had the public sector cajoling, collaborating with or threatening industry to participate. In the same time span, companies greatly increased their corporate social responsibility actions. To succeed in ensuring expanded access to medicines in emerging economies, all sectors will need to move away from the subsidy and corporate philanthropy models. The future in emerging economies will be written through applying mainstream corporate financial strategies that incorporate, *a priori,* the issue of expanded access to medicines.

The aim of this paper is to prepare the reader with sufficient information from each of the different lenses through which one can view the access to medicines issue. We hope it will stimulate vigorous discussion and debate on the role of the public sector in ensuring broad access to medicines for all citizens in emerging market countries.

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