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Emerging Market Pharmaceutical Supply

A Prescription for Sharing the Benefits of Global Information Flow

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NEW INFORMATION TECHNOLOGIES enable individuals in disparate locations to conduct cutting-edge research, to move that research into the development and testing of new medicines, to manufacture high-quality products, and to move those products to patients around the world. Conceptually, the world pharmaceuticals supply market may become increasingly competitive at all stages: basic research, product development, manufacturing and distribution. The diffusion of technological competence to major developing country actors in the pharmaceutical sector, such as India and China, as well as to more specialized actors such as Bangladesh (manufacturing) and Singapore (research), could result in a significant expansion of the pool of products available to treat disease, as well as more affordable prices to consumers.

Ownership of pharmaceutical technology resources is overwhelmingly concentrated in the OECD countries. These resources are protected by legal rights in intangibles and by regulatory and relational barriers to market access. The emergence of developing and middle-income country (hereinafter "emerging market country") competitors in the "originator"

and "generic" product supply markets will erode profits of OECD-based enterprises. To address this threat, the OECD-based Pharma companies (hereinafter "Pharma") are engaged in a multipronged strategic effort to maintain control over the global market. The first part of that strategy involves tightening control over technology assets through laws and regulations governing innovation (i.e., patents) and investment in product development (i.e., data protection). The second part of that strategy involves investment in the emerging market countries to acquire or otherwise exercise control over potential competitors. The third part of that strategy involves maintaining control over national distribution systems so as to provide an embedded source of revenues.

This chapter argues that the emergence of wider competition in the quest for new products, the development of those products, and the improvement of production technologies and distribution to patients/end users are strongly in the welfare interest of the global public. It further argues that emerging market countries are not yet at the stage in which the application of competition law will adequately promote and protect domestic pharmaceutical companies. It recommends that emerging market countries adopt industrial policies designed to promote and protect their infant pharmaceutical supply sectors. It recognizes that the United States, among other OECD countries, significantly subsidizes and otherwise protects its pharmaceutical industry and that emerging market countries cannot realistically compete with the advantages presently held by OECD industries without adopting and implementing their own industrial policy measures.

The Pharma companies are engaged in behavior that they consider to be profit maximizing. Profit maximization is argued to be a response to capital markets that allocate investment to industries in accordance with anticipated returns. Jean-Pierre Garnier, chairman of Glaxo, has made the point that the Pharma companies are not charitable institutions.[1] The interests of wider society in affordable prices and wider access to medicines require that external forces be mobilized to offset Pharma's profit-maximizing conduct, whether those forces are enhanced competition, government regulation, or public pressure from NGOs.

The development of a more competitive global pharmaceutical supply market will not be an immediate panacea for significant parts of the

world population who are unable to afford medicines, particularly newer ones. National and international policymakers will remain obligated to establish and implement mechanisms designed to make medicines available to those who cannot afford them.

Proliferation of Knowledge and Capacity

The Internet and other information flow innovations are rapidly transforming the global market for the provision of goods and services. Differentials in technological capacity between the OECD countries and developing countries are rapidly closing. India already has emerged as a significant base for computer software research and development, and the outsourcing by U.S.-based software companies of development work to India is a source of political concern in the United States. China is supplanting Japan as supplier to the world of middle-technology goods. While China's rapid ascendance as a technological power can be attributed to appropriation of OECD technological expertise, as its scientific community further absorbs that expertise it is a certainty that China will itself become a source of innovation.

The development of "new" medicines is complex and time consuming and carries a high level of risk. The costs of new pharmaceutical product development are high in comparison with those of middle-technology products. Pharma companies own the overwhelming percentage of existing pharmaceutical technology patents and data protection–based rights, as well as proprietary know-how protected by trade secrets. This technology asset base provides a very significant advantage in the development of new drugs, which often are based on existing technology. The Pharma companies have access to a large capital base in the form of existing assets, and they enjoy access to well-developed capital markets. In the United States, Europe, and Japan, the Pharma companies are connected to laboratories at well-financed universities and teaching hospitals. In the United States, the National Institutes of Health (NIH) has an annual budget of $30 billion, most of which is devoted to research on new treatments for disease. The fruits of NIH research are made available in the form of patented technologies to U.S.-based Pharma companies at very low cost.

In light of the static advantages working in favor of the Pharma companies, it will be difficult for emerging market enterprises to rapidly become competitive in the research and development of new pharmaceutical products (i.e., "originator" products). India-based pharmaceutical companies have focused on improvements to production technologies and are leaders in this area. The Indian government has increased its attention to public research and development funding, and Indian researchers are obtaining more pharmaceutical patents.[2] There is less publicly available information about the state of China's domestic pharmaceutical research and development, but there are reasons to believe that the Chinese government is increasing its attention to this sector. Chinese researchers have been responsible for the development of important new technologies in the treatment of malaria. China has a long tradition of attention to medicines and health. The University of Hong Kong, among others, has launched a program to identify the scientific basis underlying the curative properties of traditional Chinese medicines. China also acts as a major supplier of pharmaceutical chemicals to the OECD and therefore is already competent in production technology.

At the high end of the technology spectrum, Singapore has made pharmaceutical research and development a top national priority, investing substantially in the Biopolis research complex. Scientists at that complex were responsible for identifying the genetic markers of the SARS virus well ahead of the timeline generally projected for this task, and they licensed the results to Roche. The Israeli pharmaceutical industry, which so far has largely focused on generic production, is turning its attention to the development of new products. At the lower end of the technology spectrum, Bangladesh, a least-developed country, is emerging as a major producer of high-quality generic drugs.

In India there is a growing sub-industry of clinical testing subcontractors. Clinical testing of new drugs is the most expensive component of developing such products. Indian subcontractors hold themselves out as a low-cost alternative to clinical testing in the OECD markets.

While the Pharma companies maintain significant technology and capitalization advantages over the pharmaceutical industries of India, China, and other emerging market countries, there are good reasons to believe that these advantages will erode over the next decade.

Global pharmaceutical sales are in excess of $700 billion a year. The Pharma companies are well aware of the threat to their global market dominance represented by the emerging market pharmaceutical industries. They anticipated and have been acting upon this threat since the early 1980s. As the pace of change accelerates, largely based on development of new information technologies and enhanced global information flows, the Pharma response is growing in scope and intensity.

Strategic Response

Protection of Intangible Assets

OPENING ROUND

In the early 1980s, the Pharma companies initiated efforts to limit competition by tightening worldwide intellectual property standards. A failed effort at the World Intellectual Property Organization (WIPO) resulted in the shifting of the forum of negotiations to the GATT. The GATT Uruguay Round negotiations, which commenced in 1986, yielded the 1995 TRIPS Agreement, which was a qualified success from the Pharma standpoint.

The TRIPS Agreement established an obligation to provide pharmaceutical product patent protection, subject to a ten-year transitional exemption in favor of developing countries. The transition period allowed Indian manufacturers to improve their generic production technologies, although it did not provide access to the high-value OECD pharmaceutical markets when patent protection was in place there.

However, from Pharma's standpoint there were several important limitations to the TRIPS Agreement. First, it did not provide protection against the sale of generic drugs to countries where patents had not been obtained. The major Pharma companies traditionally file patent applications in a relatively small number of countries where substantial sales opportunities are foreseen or where competitive producers might emerge. This leaves a fairly wide range for competition from Indian (and other emerging market–produced) generic drugs in less affluent markets. Second, the TRIPS Agreement did not include any control over the pricing of patented pharmaceuticals. This was largely a developed-country problem. Virtually all of the OECD countries outside the United States

impose some form of control on drug prices, significantly constraining the pricing power of the Pharma companies. Third, although the TRIPS Agreement requires pharmaceutical product patent protection and data protection, the rules are not airtight. For example, the patent rules do not require countries to offer protection for *second medical indications*. They also allow significant flexibility in defining *inventive step*. This allows countries to limit the number of patents by requiring a significant level of innovation over the prior art. With respect to data, protection is required only as to "new chemical entities" and with respect to "unfair commercial use."

SECOND-LEVEL INTANGIBLE PROTECTIONS

The limitations of the TRIPS Agreements grew in importance as the pharmaceutical industries of the emerging market countries became more competitive. The best tactic for eliminating these limitations would have been negotiation of a second-generation multilateral agreement at the WTO: a TRIPS II. However, in the multilateral setting, developing countries were not interested in closing the few openings left to them by TRIPS flexibilities.

The second-best tactic was negotiation of bilateral and regional trade agreements that eliminate or restrict the flexibilities of the TRIPS Agreement. For complex reasons (explored elsewhere) developing countries have been willing to concede TRIPS flexibilities in bilateral negotiations that they will not concede multilaterally. Concessions include tightening standards of patentability, imposing data protection standards that make it difficult to register and market generic drugs, limiting compulsory licensing and parallel trade, and allowing the prosecution of nonviolation nullification or impairment claims. In the free trade agreement between the United States and Australia, U.S. Pharma companies have won the right to challenge Australian price control decisions (which are given effect through the determination of which drugs are available for insurance reimbursement).

In the bilateral and regional agreements the data protection hurdle is given effect by the national drug regulatory authority, which is responsible for granting marketing approval and registering medicines. Linking regulatory approval authority to the patent status of medicines enhances the power of the patent holder because an affirmative burden is placed

on the generic producer to overcome patent claims before it can market its drug. It also places a burden on national regulatory authorities to determine patent status, a burden that may be very difficult for the typical health regulatory authority to carry.

The effect of the second-best solution is to create additional impediments to the penetration of developing-country markets by Indian, Chinese, and Israeli generic pharmaceutical companies, among others.

Acquisition and Control of Potential Competitors

The greatest threats to OECD dominance of the global pharmaceutical market come from the potential emergence of innovator Indian and Chinese pharmaceutical companies, which will similarly be able to take advantage of IP protections, generating substantial research and development and marketing capital. India and China possess not only significant technological infrastructure but also large and growing domestic markets. Russia, Brazil, South Africa, the Ukraine, and a few other countries possess similar, though somewhat less favorable, characteristics for the development of integrated pharmaceutical sectors.

Although the agenda is just now being implemented, it is clear that the tactical move of Pharma is to employ accumulated capital stock to acquire and/or control companies based in India and other emerging market countries. This will be combined with "green-field" investments (i.e., new investments not involving existing local enterprises) in these countries. This trend is visible in Glaxo's expanding relationship with one of India's leading independent pharmaceutical companies, Ranbaxy, several of whose senior managers are former Glaxo employees. It is very difficult for independent companies in India to resist the amount of capital available to foreign multinational investors. From the standpoint of a Pfizer or a Glaxo, it is preferable to spend several hundred million dollars to acquire control of a potential competitor than to risk the emergence of a strong competitor in the global market. Novartis in 2009 announced a planned $1 billion investment over five years to upgrade its research and development capacity in China. According to Novartis, this will allow it to take advantage of the large pool of talented researchers in that country.[3]

The growing penetration of the OECD-based Pharma companies in India and China will be aided by highly paid consultants, accountants, and lawyers who earn from foreign employers fees that cannot be matched by the domestic industry. The capacity for the Pharma companies to take control of the domestic regulatory infrastructure by paying the private regulatory elite to influence government policy is a phenomenon evident throughout the developing world. The result is a new class of locally based service providers with a strong vested interest in the protection of OECD corporate interests.

Control over Distribution

The pharmaceutical supply market is multilayered. Even if a manufacturer is able to remain independent and overcome patent and data protection barriers, it must still find distributors to place its product on the national market and, in the case of prescription medicines, physicians to prescribe the medicine and pharmacists to dispense it. Although this trend has recently abated, in the United States the major Pharma companies have in some cases controlled large pharmaceutical distributors. More commonly they enter into contracts with prescription pharmaceutical distributors under which a broad range of products are supplied. There are substantial efficiencies from the distributors' standpoint in doing business with a limited group of suppliers. The capacity of the major Pharma companies to supply a broad range of products makes it more difficult for smaller enterprises, including developing-country suppliers, to enter the market. The Pharma companies spend significant amounts of money to promote their products with physicians and on direct-to-consumer advertising. Physicians receive ancillary benefits, such as vacation seminars.

The Pharma companies similarly seek to control domestic distribution systems in developing countries. In many developing countries the local Pharmaceutical Manufacturers Association is dominated by the major international Pharma companies, which play a significant role in lobbying domestic drug and health care policies.

Perhaps of most importance, the Pharma companies spend tremendous amounts of money lobbying governments around the world. In the United States, they contribute to election campaigns and lobby Congress

and the federal agencies responsible for regulating health care. The Medicare Prescription Drug Benefit program is one of the most costly government programs ever adopted. It was projected to cost the federal government $1.2 trillion over a ten-year period.[4] The terms of the program prohibit the federal government from negotiating the price of drugs with the pharmaceutical industry on behalf of the private insurance companies that give effect to the program (the so-called "non-interference clause"). This program may be one of the largest government-controlled transfers of wealth from the public to the private sector in human history.

Although there does not appear to be an explicit preference in the program for the purchase of drugs from American-based pharmaceutical companies, because the Pharma companies dominate the originator market and have established contractual relationships for the supply of generic drugs with health care providers, it seems highly likely that American-based Pharma companies will be the greatest beneficiaries of the Medicare Prescription Drug Benefit program.

Generic-substitution laws are an important tool for controlling drug prices. Such laws mandate or authorize the pharmacist to substitute generic versions of patented drugs prescribed by physicians, unless specifically directed otherwise by the physicians. The Pharma companies have argued that such laws interfere with their trademark rights. Even though generic-substitution laws are common in the OECD, including among the states of the United States, a specific challenge was made against the introduction of such a law in South Africa based on alleged trademark rights in the case brought by thirty-nine pharmaceutical companies against the government. That challenge was withdrawn (along with the other ill-founded claims).

The single most important item on the current Pharma agenda is the elimination of pharmaceutical price controls, particularly in the OECD markets, though that is also a goal rather difficult to achieve. The companies argue that because the United States does not control pharmaceutical prices while other OECD countries do control such prices, the United States is effectively subsidizing the research and development interests of other OECD countries. They argue that removal of price controls would eliminate the apparent failure of research and development burden sharing. Implicit in that argument is that prices for pharmaceu-

ticals in the United States would be lower if they were higher in other OECD countries. Because Pharma companies control the OECD market for new products, the net effect of eliminating price controls would be to increase Pharma profitability disproportionately as compared with that for emerging market producers, thereby reinforcing Pharma advantages. Fortunately, European governments that control prices do not appear likely to be persuaded of the benefits of increasing further Pharma profitability through the elimination of price controls.

Implications for Consumer Welfare

As India, China, Israel, South Korea, Singapore, and other emerging pharmaceutical research and development centers increase their capacity for bringing innovative products to market, it seems likely that the pace of innovation on a global scale will increase and the public as a whole will benefit from the introduction of new therapeutic treatments. If the diffusion of technology to emerging pharmaceutical research and development centers is sufficiently powerful, we could enter a new era of technology-based competition in the pharmaceutical sector based on a significant increase in the number of products available for treatment in a particular therapeutic class. If there are a number of competing products in a therapeutic class, even if those products are patented, an increase in price-based competition would be expected, leading to lower prices. The possibility for competition within therapeutic classes provides a good reason for preferring that enterprises in emerging markets remain independent of the Pharma companies.

To the extent that emerging market enterprises survive as independent entities, they will seek patent protection for their inventions and attempt to preserve supra-competitive rates of return for as long as possible. They will charge the price the market will bear, with particular aim at the high-value markets of the OECD. In this respect, there is no reason to assume that enterprises in emerging markets such as India and China will behave differently from OECD-based Pharma companies. Problems of access to newer medicines among poorer segments of the global population may depend not upon which country is the source of that medicine, but rather upon whether governments are willing to take steps to promote access.

The preservation of independent pharmaceutical enterprises in emerging markets is more likely to affect pricing and availability in the generic than in the originator products sector. That is, it is critical that a significant number of well-financed generic producers participate in the global supply market because this is what constrains prices and enhances availability. Because high profits from the originator products sector are used to finance the establishment of distribution arrangements in the generic sector, it is important that the emerging market independents be active in both segments of the market.[5] Independent Indian pharmaceutical companies, today mainly active in producing generic products, are deeply concerned that by acquiring significant stakes in the local market, better-financed OECD-based Pharma companies will be able to drive them out of business. If this happens, the resulting decline in generic competition will push prices up worldwide.

The greatest potential threat to global consumers of pharmaceutical products is that the OECD-based Pharma companies will succeed in foreclosing competition in the market for generic products. They may accomplish this using the threefold strategy discussed previously, namely by preserving static technological leads through strengthened intellectual property protection, acquiring and/or controlling potential competitors and dominating distribution systems.

Preserving the Fruits of Global Information Flows

The problem faced by emerging market pharmaceutical industries in competing with the Pharma companies may broadly be described as a competitive markets problem, but not in the sense that the problem may be redressed solely by the application of traditional competition law principles. There are two reasons for this. First, and perhaps most important, the Pharma companies possess very significant advantages in the form of ownership of technology and access to capital markets and government subsidies that create a playing field which is not level. It is difficult to place the problems facing emerging market pharmaceutical industries squarely within the boundaries of traditional competition law. Second, even if the problems might be redressable as traditional problems of anticompetitive conduct, there would still be considerable difficulty with redressing them.

Regarding redress of anticompetitive conduct, most developing-country governments, including those of the major emerging pharmaceutical supply enterprises such as India and China, have only rudimentary competition law infrastructures. There is very little political impetus at the international level for the development of a multilateral competition law infrastructure that might overcome weakness at the individual nation-state level. In addition, the OECD countries have adopted policies that encourage their enterprises to engage in anticompetitive conduct in developing-country markets.[6] U.S. and EU competition laws each exempt anticompetitive conduct with solely foreign effect from their scope of application.

In an ideal world, developing-country antitrust authorities would play an essential role in protecting against consolidation of power in the pharmaceutical sector. At the moment, this can be viewed as only a long-term solution that is unlikely to influence the shape of the global market during the next decade, at least.

The larger solution for the emerging market countries lies in providing infant industry protection and support that will allow their pharmaceutical companies to compete on a level playing field with those of the OECD. Such protection may combine a variety of elements of industrial policy, including but not limited to:

- Placing legal limits on the level of foreign investment penetration of the national pharmaceutical sector. This could be accomplished either by limiting the percentage of ownership or control over individual enterprises or by limiting the overall level of ownership within the domestic market.
- Establishing a framework for public investment in research and development on new pharmaceutical technologies. The U.S. NIH framework principally involves contract projects with universities and private researchers, the results of which are made available for licensing to the local private sector.
- Using the public health budget to bolster domestic production by contracting with locally owned enterprises to provide medicines.
- Limiting the use of public funds for the purchase of new foreign-developed pharmaceuticals absent a clear demonstration of improved efficacy so as to reduce public health expenditure outflows.
- Controlling the prices of originator medicines.

- Using tax policy to bolster the domestic pharmaceutical sector. The United States, for example, recently allowed a tax holiday on the repatriation of foreign-generated profits that resulted in very significant contributions to the balance sheets of domestic pharmaceutical companies.
- Selectively using compulsory licensing to enhance public access to pharmaceuticals by creating competition from locally produced generic drugs, thereby bolstering generic producer capacity.
- Gradually building up the capacity of competition regulatory authorities.

Limitations on foreign equity participation will to some extent lower capital investment in the pharmaceutical sector, at least for the short term. For countries such as India and China, the possibility for foreign investors to take minority equity stakes in domestic pharmaceutical companies should be sufficient to attract a reasonable level of investment. In any case, there is no other viable mechanism for preserving independent enterprises when confronted with foreign investors holding enormous stocks of capital. However, the possibility for underinvestment by foreign enterprises makes it important to combine limitations on foreign equity participation with positive government policies in favor of locally owned enterprises, such as research and development subsidies and tax incentives.

There are important recent examples of infant industry promotion used to establish strong domestic industries. These include the European civilian aircraft sector, the Korean steel sector, and the Japanese supercomputer sector. Because the United States provides such heavy subsidies and incentives to its pharmaceutical industry, emerging market countries will not be able to establish and maintain competitive industries in the absence of comparable countermeasures. Such countermeasures could well be viewed as transitional arrangements until the playing field becomes more level and the means for regulating and preserving competitive markets emerges.

The Role of Governments in Protecting the Poor

As noted at the beginning of this chapter, it is unlikely that developments in the global pharmaceutical market over the next decade will provide substantially enhanced access to pharmaceutical products for the poorest

segments of the world's population. That part of the world's population is not a functioning "market" in the sense that financial demand will induce adequate supply. There are a variety of tools that government policymakers can use to correct this market failure. This includes transfer payments such as underlay operation of the Global Fund, compulsory licensing of patents to allow lower-cost production for newer products, and bulk procurement arrangements to take advantage of economies of scale. Differential pricing may play a role, although care must be taken that it not be used as a means to allow dominant-market actors to foreclose the emergence of competitors. Funding for public development partnerships (PDPs) that focus research and development on "neglected diseases" must be placed on a sustainable footing.

Over the next decades a wider geographic distribution of research and development activities will, one hopes, result in an increased pace of discovery and the emergence of a more competitive global pharmaceutical supply market. Competition should bring prices down, improving access across all parts of the world's population. This chapter argues that vigilance and affirmative action are necessary for that new global environment to evolve.

Notes

1. "The furor surrounding Glaxo Smithkline chief executive Jean-Pierre Garnier's massive pay package led to an embarrassing defeat at the AGM and a public perception that all pharmaceutical executives are 'fat cats.' 'I'm not Mother Teresa' was his calm response to the situation, which prompted ridicule from areas as diverse as AIDS charities worldwide and popular news quiz Have I Got News for You." *Are the drug giants in danger of bleeding themselves dry? The pharmaceutical sector is beset by rising costs and bad PR* THE DAILY TELEGRAPH (LONDON), October 09, 2004.

2. See presentation by Dr. Ramesh Mashelkar (Council of Scientific and Industrial Research, India), *Human Development and Pharmaceutical Development, with special reference to TRIPS and India*, National Institutes of Health, Globalization, Justice and Health Conf., Wash., D.C., Nov. 4–5, 2003.

3. Novartis Media Release, *Novartis announces USD 1 billion investment to build largest pharmaceutical R&D Institute in China*, November 3, 2009. See also *Novartis Institute of Biomedical Research, Zhangjiang Hi-Tech Park, Pudong New Area, China*, http://www.pharmaceutical-tecnology.com/projects/novartis-institute (accessed December 12, 2009).

4. Ceci Connolly and Mike Allen, *Medicare Drug Benefit May Cost 1.2 Trillion, Estimate Dwarfs Bush's Original Price Tag*, Wash. Post, Feb. 9, 2005.

5. Competition among generic producers drives down price, and this effect becomes more pronounced as a significant number of producers compete in the supply of the same product.

6. See Frederick M. Abbott, *Are the Competition Rules of the WTO TRIPS Agreement Adequate?*, 7 J. Int'l Econ. L. 682 (2004).

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