TRIPS And The Global Pharmaceutical Market

Can the pharmaceutical industry make drugs available to developing countries without compromising its research incentive?

by John H. Barton

ABSTRACT: This paper reviews the international controversy over patents and access to drugs in developing countries and explores the implications of the 1995 Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement, the 2001 Doha Declaration, and the 2003 agreement preceding the Cancun meeting. These agreements do not resolve the important funding issues that developing countries confront as they seek access to drugs. Also, the international debate and its resolution will complicate the importing of foreign pharmaceuticals into the United States and strengthen pressures both for expanding public support of U.S. drug purchases and, in the long run, for political control of U.S. pharmaceutical pricing.

FOR THE PAST SEVERAL YEARS there has been a widespread, bitter debate over access to pharmaceutical products in developing countries. The debate has focused largely on access to antiretroviral agents for HIV patients in sub-Saharan Africa. A group of nongovernmental organizations (NGOs) has argued that patents on these drugs in the developing world raise the prices of the products necessary to help such patients survive, whereas the research-based pharmaceutical industry has argued that many of the relevant products are not on patent in the countries involved and that the problem is not patents but inadequacy of the medical infrastructure.[1]

Sources Of The Debate

The pharmaceutical industry views the patent system as essential to its business model. Under the basic concept of the patent system, an inventor is entitled to a limited monopoly (technically, a right to exclude) for a period of time, typically twenty years. Such exclusivity may permit high prices during the patent term; the consequent profit incentives provide the basis for the pharmaceutical industry to invest in the very costly development process that is necessary to bring new drugs to market. The first generation of patients (or their employers or insurers or, in some cases, the government) pays in this way for the large research costs

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involved in developing a new drug. When a patent expires, the price normally falls as generic competitors enter the market.

A number of developing countries, however, viewed patent law quite differently and deliberately decided to deny patent protection to pharmaceutical products and to grant protection only to processes for producing pharmaceuticals. These countries believe that access to pharmaceutical products is so important that the products themselves should not be patented. The products would be developed anyway for the market in developed countries, and the market in developing countries is so small that it would not provide adequate incentive to develop new products.

In its 1970 patent law, for example, India excluded drugs from product patent protection, effectively choosing to provide low-cost drugs for its people at the expense of eliminating incentives to create new products. This law was one of the reasons that the Indian generic drug industry was able to evolve to make and market copies of drugs still on patent in wealthier countries. India has become a major international supplier of drugs to countries where these products can be marketed legally because they have not been patented locally. Also, a number of countries had "compulsory licensing" provisions. These provisions define a legal process under which governments can authorize use of a patented technology even over the patent holder's objection. In practice, compulsory licenses have rarely been formally granted; rather, governments have used the threat of granting a compulsory license as a way to negotiate lower prices for the technology or product involved.

■ **TRIPS responds.** The United States and other developed countries were determined to change these laws and achieved important extensions of patent protection in the Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreement, which entered into force 1 January 1995. This agreement requires the member nations of the World Trade Organization (WTO)—which includes nearly all major trading nations—to live up to defined standards of intellectual property protection. The proponents of TRIPS were responding to pressure from their pharmaceutical, copyright content, and trademark-based industries. These industries viewed themselves as victims of "piracy" in many markets throughout the world and wanted to gain increased protection for their products. Developing countries accepted the agreement—which they recognized would greatly increase their royalty and license costs—in return for developed-world concessions that would expand these countries' exports of agricultural and textile products.

The most important provision of TRIPS with respect to pharmaceuticals, Article 27, requires that "patents shall be available for any inventions, whether products or processes, in all fields of technology." The clear intent was to prohibit exclusions of drug products such as those contained in the Indian law. Another very detailed article, Article 31, establishes procedural limitations on when a country can grant a compulsory license. As part of the political compromise, there are

transitional provisions, which allow developing countries extra time to comply with the treaty requirements and also create arrangements for the remaining parts of patent terms to be made available for products developed during the transition periods. Because of these transition provisions, India, along with a number of other countries, is not required to provide product patents on pharmaceuticals until 1 January 2005.

■ **NGOs weigh in.** During the late 1990s a group of nongovernmental organizations (NGOs), including, for example, Oxfam and Médecins sans Frontières, argued that the requirements of patent law, especially in sub-Saharan Africa, led to increased prices, particularly of antiretrovirals that might be used against HIV. Two particular disputes intensified the tensions. One arose from a South African law to import generic antiretrovirals, even of drugs patented in South Africa. Such import, for use in South Africa, is arguably an infringement of South Africa patent law. The international pharmaceutical industry attacked this law in the South Africa courts. The suit became a public relations debacle for the industry, and after threats that the amount of public support for the development of the relevant drugs would be publicized in the hearings, the industry settled in April 2001.

■ **Brazil fights back.** The other dispute involved Brazilian production of antiretrovirals in pursuance of its national campaign of attempting to treat all HIV patients needing such drugs. This campaign originally relied on imported drugs but became increasingly expensive as the Brazilian currency fell. Brazil therefore manufactured some of the off-patent drugs in its own laboratories and greatly reduced the costs. Its threat to do the same for certain patented drugs in 2001 (through what would have effectively been a compulsory license) led to negotiated lower costs for the import of these drugs. The United States threatened Brazil before the WTO, arguing that Brazilian law violated TRIPS, but agreed in July 2001 to put the dispute into bilateral discussions.

The Agreements Of 2001 And 2003

■ **Advent of differential pricing.** These disputes led to international agreements that are based on a compromise that prices should be lower in developing than in developed countries, permitting drug firms to recover their research spending through high prices in the developed world while making products available at lower prices that are near actual production cost to the poor in developing countries. This approach is justified because the market in poor countries is so small that it provides only a minimal incentive—the total market of the poorest countries (for example, sub-Saharan Africa or the United Nations' Least Developed Countries) is on the order of 1 percent of the global pharmaceutical market. Moreover, for many, it is inequitable to expect a poor person in the developing world to provide the same contribution toward research costs as is provided by a rich person in a developed country. Certainly, the actual production cost of a dose of a product is essentially the same for any market, but the logic of the patent system is to permit an elevated price

to allow recovery of research and development (R&D) costs. It seems reasonable that the burden of these costs, which benefit all of humanity, should fall more heavily on the wealthy than on the poor. The research-based pharmaceutical industry would prefer to achieve this differential pricing by a donation program or by simply charging different prices. Critics would prefer that the patent monopoly not be available to raise prices in the developing world.

■ **Doha Declaration.** Brazil and a group of African countries, working with the NGOs, brought the issue of TRIPS and drug access to the global debates preceding the Doha (Qatar) meeting, a November 2001 meeting of the world's trade ministers to organize a new round of trade negotiations. The meeting led to the Doha "Declaration on the TRIPS Agreement and Public Health." This declaration affirmed that TRIPS "should be interpreted and implemented in a manner supportive of WTO members' right to protect public health and, in particular, to promote access to medicines for all." It affirmed the right of nations to use the exceptions of TRIPS, such as the compulsory licensing provision discussed above, to meet public health concerns, specifically stating that "public health crises, including those related to HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency" and thus facilitate the right to use compulsory licensing.[2] This was regarded as a victory by the developing world and as a defeat by the research-based drug industry.

The Doha Declaration left a technical legal problem unresolved. This problem, known as the 31(f) problem after the relevant provision of TRIPS, involves the manufacture of drugs under compulsory license for countries that lack the capability to manufacture the drugs themselves.[3] By the end of 2002 all relevant countries except the United States had agreed to a procedure to solve the problem by waiver of Article 31(f). The procedure covered products needed to meet the public health problems recognized in the Doha Declaration, but the United States feared that it would be expanded to a broad variety of products and thus was unwilling to accept it. A compromise was finally reached in August 2003, under which the United States accepted the 2002 document, provided that the chairperson of the General Council of the WTO parties would make an appropriate parallel statement. The chairperson made the statement, which included language that the agreement would be used "in good faith to protect public health" and not be "an instrument to pursue industrial or commercial policy objectives" and recognized the need to respond to the industry's concern that products produced under this agreement not be exported to major developed-world markets.[4]

Evaluation From The Viewpoint Of Developing Countries

This agreement represents a step forward for access and will certainly place pressure on the research-based pharmaceutical industry to provide products in the developing world at low prices. Yet several problems remain unsolved.

■ **Inadequate solution for AIDS patients.** Most importantly for the developing world, resolving the legal problem of Article 31(f) does not really resolve the eco-

nomic one. Under the current system, under which copies of patented drugs can still be made by Indian firms, only about 1 percent of sub-Saharan Africa HIV/AIDS patients are receiving antiretrovirals, partly from purchases of brand-name products, partly from generics, and partly from donations by brand-name manufacturers.[5] To provide drugs to all patients who now need such treatment for HIV and other epidemic diseases throughout the developing world, even if the drugs are available at low prices, requires amounts beyond the level of any currently available global funds. The World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) estimate that six million people with HIV in developing countries need antiretroviral therapy.[6] Even at the reduced prices approaching $300 a year for antiretroviral combination therapies, this would amount to $1.8 billion and would use a very substantial portion of President George Bush's $15 billion (over five years) HIV initiative. But this is just one disease. The pharmaceutical industry is absolutely accurate in its criticism that patients in developing countries do not receive adequate access to even those drugs that have long since been off patent and are available in much of the world at relatively low prices.

■ **Affordability of Indian drug-industry products.** Moreover, after 2005 the Indian generic drug industry, which has been the supplier of a portion of the sub-Saharan Africa market, may no longer be able to manufacture products that are still under patent; it will have to become like the generic industry elsewhere—making products that have gone off patent. Certainly there will be cases where the Indian government can issue a compulsory license to enable local generic versions of patented products to be manufactured for the Indian market, but under TRIPS this cannot be done as a matter of routine. The important implication arises from the fact that a new manufacturer cannot start to produce new patented products under a compulsory license without incurring start-up costs to cover, for example, developing a production process, testing to demonstrate bioequivalence, and building or leasing facilities to actually produce the product. These fixed costs, which vary from drug to drug—depending, for example, on whether important active ingredients are available or must be manufactured—must ultimately be reflected in the price of the product. Also, their impact on the price depends on the size of the market; presumably a Brazilian or Indian national market can absorb them without a major price effect, but a small sub-Saharan African country probably cannot. The fact that such a country has the legal right to obtain a product does not mean that it can afford the product, particularly if large start-up costs must be covered and cannot be shared with other countries.

Hence, the global solution almost necessarily involves increasing funding; the situation is far from being resolved by the legal maneuvering surrounding the Doha Declaration. The problem will become more complex as the required changes to Indian patent law affect the Indian pharmaceutical industry's ability to produce on-patent products after 2005.

■ **Strategies to cover manufacturing costs.** There are two general strategies

for product manufacture at reduced prices for developing countries. One is to work with the major pharmaceutical firms, either by requiring them to provide products at near-production cost to patients in developing countries or by purchasing products from them at developed-world market cost and distributing them in the developing world at a subsidized price. It is probably not in the drug industry's economic interest to price differentially, but the industry could be persuaded to do so on the basis of its own sense of public service, especially if combined with specific legislation or with the threat of compulsory licensing.[7] (The industry already supplies donations.)[8] Most likely, the international donors—probably primarily the taxpayer in the developed world—will pay a price that covers the production cost and a portion of the R&D costs of the product. For vaccines, international entities already obtain products for the developing world at enormous discounts with prices on the order of $0.50 per immunized child.[9]

The alternative approach is to produce the products under compulsory license either in a private-sector generic industry, whose fixed costs are distributed over a fairly large market, or in a public-sector generic industry, whose fixed costs are covered by the public. This approach offers competition as a way to lower prices, rather than necessarily requiring dependence on an administrative determination of an appropriate price. Moreover, it might offer new opportunities for production within the developing world, something that would be extremely popular politically with economic leaders of developing countries. Having the threat of the second approach could make the first approach more possible or decrease the cost to donors. It is also possible that India—or a global entity—might choose to subsidize the fixed costs (or at least permit these costs to be covered by higher prices to Indian consumers) so that an Indian industry can export to poorer developing countries at a reasonable price. There is already a debate in Canada over ways to encourage the Canadian industry to produce generic drugs for export, and a bill has been introduced to facilitate this process.[10]

■ **Impact on industry incentives.** The Doha/Cancun resolution may also affect drug-industry incentives for the development of new drugs. The possibility that prices will be forced down by compulsory licenses in developing countries weakens the incentives to develop products for these markets. These incentives are already low, however, because the total magnitude of the developing-world market for products for HIV, malaria, tuberculosis (TB), or less widespread diseases is likely to be too small to be an adequate incentive for the private sector under any circumstances. To respond to this problem, a variety of nonprofit public-private partnerships, such as the International Aids Vaccine Initiative, the Medicines for Malaria Venture, and the Global Alliance for TB Drug Development, are now in place. These efforts involve public or donor funds and often work in cooperation with the private sector. So far, they are working at the research level; when they succeed, they will face the same problem of financing production and distribution.

For new products for the developing world, such as those for malaria, TB, and

some HIV strains, where there is relatively little developed-world market, patients in developing countries or the world public sector must pay for the development costs at some point, either during the research phase or later on at higher prices during the market phase. At one extreme, the public and donor sectors can support private-sector product R&D, conditioned upon charging of a reasonable or preferential price at the time the product is actually provided. At the other extreme, there have been suggestions for funds that would be big enough to guarantee a market for new products designed for developing-world needs.[11] Assuming that the promised price was high enough, the private sector would have the incentive to invest in the necessary research. Very difficult issues exist in defining the conditions under which the fund would purchase and in making a strong enough promise that industry would actually invest in the development of products tailored to this artificial market.

■ **Funders' choice.** Realistically, there may never be an overall explicit choice of one of the strategies over others, save perhaps for a few cases of specific diseases in specific regions. After all, the funding is highly decentralized: some patient payment; developing-world national health systems; international donors such as the World Bank and developed-world taxpayers supporting these national health systems; public-private partnerships; the Global Fund to Fight AIDS, Tuberculosis, and Malaria, created in January 2002, which has already spent about $600 million; special funds such as the $15 billion proposed by President Bush for HIV over five years; and important private donors such as the Bill and Melinda Gates Foundation. The effective decisions will be those defined by the purchasing policies of these organizations, choices already exemplified in the policies of the Global Fund and of the UNICEF Supply Division in its procurement of childhood vaccines for developing countries. Will these entities buy drugs from pharmaceutical firms at developed-world market prices or at lower prices, effectively following the first strategy above? Or will they buy from generic manufacturers, perhaps contributing to the evolution of manufacturing in developing countries? How will they balance their efforts between purchase of existing drugs and development of new ones? The existing purchasing system is strong enough generally to provide vaccines (where these exist) and also strong enough that the industry is sometimes willing to offer lower prices in return for the confidence of having a major market and of being paid. But it is far from strong enough to cover all reasonable needs or to make the kind of commitment needed to encourage the private firms to invest on a large scale in research for the special needs of the developing world.

Issues For The United States

These trends and the recent agreements, clearly most important for the developing world, will likely have major impacts on the United States and the rest of the developed world as well. One impact arising from the differential pricing concept is the need to prevent import of the low-price products into the developed

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world. Such imports would cut into the patent-protected market of the developed world and therefore affect incentives to develop new products. Yet a number of local entities in the United States are already looking to Canada as a source of less costly pharmaceuticals, and the possibility of obtaining less costly drugs from abroad is a staple of U.S. congressional debate, which so far has been fairly successfully staved off by the pharmaceutical industry.

The backflow issue is partly a practical problem. The purchases from Canada derive from rather small price differences together with easy travel. The price differences with respect to the developing world are likely to be much larger so that reverse flow will be more tempting—but, as a practical matter, it will be much harder to take advantage of the price differences between Africa and the United States than of those between Canada and the United States. Travel is much more difficult, and, in the African case, it may be easier to control sales over the Internet by controlling the physical entry of the products. Industry will certainly use patent and trademark law to attempt to restrict the import of products into the developed world and to make sure that low-cost products provided to the developing world are distinctive in color or packaging. It will also attempt to control the distribution of products in the developing world, to avoid diversion through corruption and the risk that products will be misused in a way that contributes to the emergence of drug resistance.

But what will probably be more important is the political backflow. As it becomes public knowledge that a product is available to the poor—or, of greater political import, to the rich—in a developing country at a price far below that which a U.S. pensioner must pay, the backlash for the pharmaceutical industry will be severe. Certainly there will be efforts to justify to the U.S. public the low developing-nation prices on humanitarian grounds, but ultimately the only real political response is probably a U.S. program to subsidize the purchase of drugs for the U.S. public. It is not at all clear that the arrangements created by the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) of 2003 will be adequate to solve this problem. After all, the drug benefit under this provision is still quite limited.

The new issues will go beyond the pressure for subsidized drug access within the United States. The debate about developing-world prices is making the workings of drug pricing more transparent, which is likely to make it an even more a political issue than it is now. Moreover, the United States has not yet dealt with the fact that because of their national price controls, European (and Canadian) patients pay a smaller share of R&D costs than U.S. patients pay.[12] It is hard to imagine that there will be substantial and explicit dependence on public funding for

the world's drug needs without there also being a move toward public-sector control of the price. The new Medicare act has provisions to protect the drug industry's pricing arrangements from government review, but it is hard to imagine that the taxpayers will long deny themselves the right to negotiate for lower prices.[13] If there is price control, it will have to be done in a way that protects the incentives for investment in research.

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NOTES

1. See U.K. Commission on Intellectual Property Rights, *Integrating Intellectual Property Rights and Development Policy* (London: CIPR, September 2002), especially Chapter 2. For the NGO perspective, see Médecins sans Frontières, "Drug Patents under the Spotlight," May 2003; and Campaign for Access to Essential Medicines, www.accessmed-msf.org/index.asp (3 January 2004). For the industry perspective, see the International Federation of Pharmaceutical Manufacturers Associations, www.ifpma.org (3 January 2004). For more academic perspectives, see B. Pécoul et al., "Access to Essential Drugs in Poor Countries: A Lost Battle?" *Journal of the American Medical Association* 281, no. 4 (1999): 361–367; and A. Attaran and L. Gillespie-White, "Do Patents for Antiretroviral Drugs Constrain Access to AIDS Treatment in Africa?" *Journal of the American Medical Association* 286, no. 15 (2001): 1886–1892. The proceedings of the important WHO/WTO Workshop on Differential Pricing and Financing of Essential Drugs, at Hosbjor, Norway, in April 2001, are at www.wto.org/english/tratop_e/trips_e/hosbjor_presentations_e/hosbjor_presentations_ e.htm (13 February 2004).
2. World Trade Organization, "Declaration on the TRIPS Agreement and Public Health," 20 November 2001, www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.htm (17 February 2004).
3. Article 31(f) of TRIPS requires that manufacture of products under compulsory license be predominantly for the domestic market. Thus, a small sub-Saharan African country that clearly has the right to grant a compulsory license may have no local industry able to manufacture the product. If it asks a foreign firm to manufacture the product, that firm might be manufacturing the product primarily for export—a result that would violate TRIPS.
4. See WTO, "DOHA Development Agenda: Decision Removes Final Patent Obstacle to Cheap Drug Imports," 30 August 2003, www.wto.org/english/news_e/pres03_e/pr350_e.htm (13 February 2004).
5. UNAIDS, *Accelerating Action against AIDS in Africa* (Geneva: UNAIDS, 1 September 2003), available for download at www.unaids.org.
6. World Health Organization, *The Three by Five Initiative* (three million patients by 2005), www.who.int/3by5/en (13 February 2003).
7. F.M. Scherer and J. Watal, "Post-TRIPs Options for Access to Patented Medicines in Developing Countries," January 2001, www.cmhealth.org/docs/wg4_paper1.pdf (13 February 2004).
8. See, for example, International Federation of Pharmaceutical Manufacturers Associations, "African Comprehensive HIV-AIDS Partnership," 2004, www.ifpma.org/Health/hiv/health_achap_hiv.aspx (13 February 2004).
9. S. Jarrett (UNICEF Supply Division), "Vaccine Purchasing," www.unicef.org/immunization/expert_purchase.html (13 February 2004).
10. Bill C-56, *An Act to Amend the Patent Act and the Food and Drug Act*, First Reading, 6 November 2003.
11. M. Kremer, "Creating Markets for New Vaccines: Part I: Rationale, and Part II: Design Issues," in *Innovation Policy and the Economy*, vol. 1, ed. A.B. Jaffe, J. Lerner, and S. Stern (Cambridge, Mass.: MIT Press, 2001); and J. Barton, "Financing of Vaccines," *Lancet* 355, no. 9211 (2000): 1269–1270.
12. See Speech by Mark B. McClellan (then FDA commissioner) before the First International Colloquium on Generic Medicine, 25 September 2003, www.fda.gov/oc/speeches/2003/genericdrug0925.html (13 February 2004).
13. 42 U.S. Code sec. 1860D-11(i), as inserted by P.L. 108-173, sec. 101 (2003).