INTELLECTUAL PROPERTY RIGHTS AND GLOBAL HEALTH:
CHALLENGES FOR ACCESS AND R&D

global health forum II

CONSENSUS STATEMENT

ORGANIZED BY:

COMMISSION ON MACROECONOMICS AND HEALTH

INSTITUTE FOR GLOBAL HEALTH

THE WELLCOME TRUST

INSTITUTE FOR igh GLOBAL HEALTH

INTELLECTUAL PROPERTY RIGHTS AND GLOBAL HEALTH:
CHALLENGES FOR ACCESS AND R&D

global health forum II

Hinxton Hall Conference Centre
The Wellcome Trust Genome Campus
Hinxton, Cambridgeshire, UK
7–9 December 2000

CONSENSUS STATEMENT

ORGANIZED BY:

COMMISSION ON MACROECONOMICS AND HEALTH

INSTITUTE FOR GLOBAL HEALTH

THE WELLCOME TRUST

WITH SUPPORT FROM:

BILL AND MELINDA GATES FOUNDATION

ROCKEFELLER FOUNDATION

WORLD HEALTH ORGANIZATION

University of California Berkeley & San Francisco

Foreword

This report is based substantially on discussions held at the Global Health Forum II: "Intellectual Property Rights and Global Health: Challenges for Access and R&D." The second Global Health Forum was organized and convened by the Wellcome Trust, the Institute for Global Health, and the Commission on Macroeconomics and Health.

Forty representatives from private industry, governments, research funders, multilateral and bilateral organizations, nongovernmental organizations, and universities came together on December 7–9, 2000 at Hinxton Hall on the Wellcome Trust Genome Campus near Cambridge, UK. The meeting followed from the first Global Health Forum on "Creating Global Markets for Neglected Drugs and Vaccines: A Challenge for Public-Private Partnership," held at Quail Lodge, Carmel, California, on February 18–21, 2000. Some of the same participants attended both meetings.

Participants at the Hinxton Hall meeting came from the World Health Organization (WHO); the World Trade Organization (WTO); the World Intellectual Property Organization (WIPO); the European Patent Office; the International Federation of Pharmaceutical Manufacturers Association (IFPMA); the European Federation of Pharmaceutical Industries Association; the European Generic Medicines Association; the UK government's Cabinet Office and Department for International Development (DFID); the Office of Health Economics; the Bill and Melinda Gates and Rockefeller Foundations; the Nuffield Council on Bioethics; the Universities of Buenos Aires, California, Cambridge, Harvard, Pennsylvania, and Stanford; the Massachusetts Institute of Technology; the International Vaccine Institute (IVI); the British Technology Group (BTG); the International AIDS Vaccine Initiative (IAVI); the Medicines for Malaria Venture (MMV); the government of Cuba; the US National Institutes of Heath (US NIH); the South African Medical Research Council; the biotechnology and pharmaceutical industries; Médicins Sans Frontières (MSF); and the three convening organizations. (Appendix A provides a full list of Forum participants.)

This report was prepared by Carol Anne Medlin of the Institute for Global Health and the Commission on Macroeconomics and Health and Hannah Kettler of the Office of Health Economics. The authors would like to acknowledge the detailed comments and technical assistance provided by Patricia Danzon, Adrian Otten, Ariel Pablos-Mendez, and Jayashree Watal. John Barton, Donna Ghelfi, Jenny Lanjouw, Richard Mahoney, Olga Moreno Samper, Rachel Nugent, Elizabeth Stoller, Els Torreele, David Webber, and Karen White also provided helpful feedback on an early draft of the report. Miriam Polon provided excellent editorial assistance.

The Wellcome Trust has had a special interest in diseases of developing countries for over 60 years within its mission to foster and promote research with the aim of improving human and animal health. As part of an increasing move to bring the results of this research to benefit health more directly, the Trust has supported the development of candidate vaccines and drugs in affected tropical countries. Clearly, intellectual property is one issue that could affect the manner in which practical benefits accrue from biomedical research. The Trust was therefore keen to support this workshop and build on an earlier Trust sponsored meeting on intellectual property rights and genomics.

The Institute for Global Health of the University of California, Berkeley and San Francisco, is deeply committed to addressing issues of international policy and action to reduce the massive burden of disease and premature death among the world's poor. Among these issues, intellectual property has recently become a central and highly controversial topic, fueled especially by concerns regarding the price and availability of anti-retroviral drugs in Africa. Much of the public debate on this issue has been polarized and factually distorted and has not contributed to resolution of the complex and important issues at stake. Through its series of Global Health Forums, and in other ways, the Institute for Global Health seeks to contribute to the clarification of policy and the harmonization of action.

The Commission on Macroeconomics and Health was created in early 2000 by the Director-General of the World Health Organization, Gro Harlem Brundtland, to contribute to a heightened global understanding of the links between health, development, and economic policy. Eighteen commissioners will deliberate for two years, supported by six Working Groups. Two of these Working Groups (nos. 2 and 4) have terms of reference that include issues of intellectual property, access to health products, and incentives for research and development. On behalf of the Working Groups, which are chaired by Commissioners Isher Judge Ahluwalia, Richard Feachem, and Jeffrey Sachs, the Commission co-sponsored this important meeting.

We stress that this report is a good-faith attempt to represent the views of the participants at the meeting and to add information that has subsequently become available. It does not necessarily represent the views of all individual participants or of the three convening organizations. On behalf of the Wellcome Trust, the Institute for Global Health, and the Commission on Macroeconomics and Health, we hope that this report will contribute to the great challenge of bringing the fruits of advances in biomedical science and biotechnology to all people in the world who need them.

Dr. Richard G. A. Feachem
Director
Institute for Global Health
University of California
San Francisco and Berkeley

Dr. Richard Lane
Head, International Programmes
The Wellcome Trust
London

TABLE OF CONTENTS

Executive Summary

Health disparities between populations of rich and poor countries are very wide. Average life expectancy at birth in the poorest countries is only half of that in the richest. And the problems are worsening. The AIDS epidemic has taken a serious toll in sub-Saharan Africa, reducing average life expectancy by over 10 years in some countries. Multi-drug resistance is increasing in many parts of the developing world—threatening to undermine the effectiveness of the current artillery of drugs used to combat tuberculosis and malaria. As the rich countries benefit from rapidly advancing technologies in health, poor countries of the world are falling behind.

Responses to this growing crisis must take into account poor people's access both to *existing* and *future* drugs, vaccines, and diagnostics. On the one hand, the international health community desires to promote access to existing products for the people who need them at affordable prices. On the other, it wants to stimulate the development of new products targeted specifically at the diseases of the poor. These important goals are tightly interrelated.

Intellectual property rights protection is the critical element that gives rise to the interrelationship between access and R&D incentives, and this is the primary focus of this report. The spotlight is on whether current systems of patent protection, both domestic and international, strike the correct balance between creating incentives for drug discovery and development and ensuring affordable access to existing and patentable products. Other critical factors relating to access that are not treated extensively in this report include adequate financing, appropriate supply and distribution networks, and well-organized health care systems.

To develop a better understanding of linkages between intellectual property rights and public health, the Wellcome Trust, the Commission for Macroeconomics and Health, and the Institute for Global Health jointly convened a meeting entitled "Intellectual Property Rights and Global Health: Challenges for Access and R&D." The meeting was held on December 7–9, 2000 at Hinxton Hall on the Wellcome Trust Genome Campus, near Cambridge in the UK. Representatives from all the major stakeholders attended: the research-based and generics pharmaceutical and biotechnology industries of the high- and middle-income countries; governments; academics; public-private partnerships; the US National Institutes of Health; the Wellcome Trust; the World Trade Organization (WTO); the World Health Organization (WHO); and nongovernmental organizations.

Participants at the meeting were generally sympathetic to the argument that protection of pharmaceutical innovation in the form of patent rights is required to stimulate private-sector investments in R&D. But they were not in complete agreement about how far these patent rights should be extended and whether intellectual property is the appropriate tool for addressing the larger problem of incentives that skew scarce investment resources toward the diseases of the rich.

A major focus of discussion at the meeting was on the impact of the TRIPS (Trade-Related Aspects of Intellectual Property Rights) Agreement on access and R&D. TRIPS was one of the agreements reached at the conclusion of the 1986–1994 Uruguay Round of the GATT Multilateral Trade Negotiations. It is part of a package of agreements that countries must sign up to when they join the WTO. TRIPS came into force on January 1, 1995, but the transition periods for its implementation are staggered for countries at different levels of economic development.

With a few exceptions, participants found that they agreed on the following points:

- **IP protection is necessary but not sufficient for innovative R&D, especially in the area of neglected diseases.** The R&D process is lengthy and risky, but most pharmaceutical products are relatively cheap to produce after they have been discovered and developed. This feature is what permits generic firms to launch products at prices well below the cost of a branded product, following expiration of the patent. Without patent protection and a secured period of market exclusivity, generic products would enter the market immediately upon product launch, and force prices down to marginal cost. Since marginal costs do not cover the fixed costs of R&D, the likely result would be a decrease in R&D and hence a decline in the number of new products brought to market.

Therefore, IP protection is needed to encourage risk-taking and innovation in the large research-based pharmaceutical companies and biotechnology firms.

- **TRIPS will affect developing countries differently, depending in part on the current state of development of their pharmaceutical industries.** Some countries such as India will be ready to compete in global markets, shifting away from the "copycat" strategy of producing patented products without authorization toward a research-based strategy of discovering and developing new products. Still, there is little evidence to suggest that TRIPS will increase the amount of investment directed toward neglected diseases. The expectation that it would is based on the assumption that local companies could discover and develop drugs at a fraction of the cost of global players and thus make a "neglected disease" strategy profitable, despite the low purchasing power of consumers. Volume sales of low-priced products could pay off if the R&D costs are sufficiently low.

  The basis for this proposition seems weak for a number of reasons. First, to realize these optimistic cost savings, significant investments in drug discovery and development are needed. Such cost savings also depend on a steep and rapid learning curve for companies that, with few exceptions, have until now done little or no extensive R&D of the type required to discover, develop, and market new products. Second, even if companies were capable of realizing such low costs, money-making opportunities from diseases of the rich will be many times greater than those from neglected diseases. Not surprisingly, Cipla and Ranbaxy, two of the largest research-based pharmaceutical firms in India, have targeted global markets by focusing their research on conditions of concern to the wealthy and aged, including cardiovascular disease, diabetes, and cancer. A 1999 survey of Indian firms indicated that only 16 percent of R&D expenditures were targeted at tropical diseases.

- **Certain flexibilities within TRIPS—including compulsory licensing and parallel importing—could permit countries to obtain patented pharmaceutical products more cheaply.** Although these options are available to countries under TRIPS, they are far from ideal solutions to the complicated problem of gaining access to affordable drugs, diagnostics, and vaccines. Legal wrangling over compulsory licensing is likely to be costly, and long licensing delays will work strongly to the disadvantage of countries seeking to obtain licenses. The process of reaching agreement on appropriate royalty payments may also be difficult. Finally, parallel importing itself does not appear to be optimal from a long-term perspective. Economic theory suggests that prices will tend to converge to a single global price if parallel importing becomes widespread. While rich countries may ultimately pay less for pharmaceuticals than they would have in a world without parallel imports, poor countries will pay more as prices converge across all markets. Further, a single uniform price for all developing countries, irrespective of income levels, may work to the disadvantage of the poorest countries. Neither compulsory licensing nor parallel importing are stable solutions, and they may undermine incentives for private-sector investment in the neglected diseases.

- **Differential pricing offers a way to improve access without harming R&D incentives.** Under differential pricing arrangements, consumers in rich countries bear the costs of R&D by paying higher prices for pharmaceutical products than consumers in developing countries (who pay only the manufacturing costs, minus overhead). Certain guarantees must be set in place for differential pricing to be implemented effectively. These include preventing a backwash of cheap products from the developing to the developed countries; preventing the use of cheap prices offered to poor countries as reference prices for government purchases of drugs in rich-country markets; identifying the true marginal costs of production in the absence of generic production and in the absence of full knowledge of industry's R&D costs; and sustainable financing. However, it is important to remember that although differential pricing provides an approach to improving access without compromising R&D goals, it does not directly address the problem of incentivizing R&D in areas of particular concern for poor people in developing countries. In fact, differential pricing can be applied only when there is an overlap between rich and poor markets for drugs, since otherwise the costs of R&D will not be borne by consumers in rich countries. Other strategies will be needed for the diseases that affect only the developing countries (e.g., the tropical diseases such as sleeping sickness and river blindness).

IP can be used creatively to simultaneously stimulate R&D investments and address barriers to access. Participants at the meeting reviewed a variety of creative strategies that use IP as an instrument for achieving the twin objectives of stimulating R&D and improving access to products, drawing on the unique strengths of both the public and private sectors. These include the use of "defensive patenting" by the Wellcome Trust and White Knight provisions by the US National Institutes of Health. The goal of these strategies is to maximize the social returns on public sector funding of health research.

Many of the public-private partnerships represented at the meeting seek to use innovative IP arrangements and public funds to attract private industry involvement in developing new pharmaceutical products for the poor in developing countries. The changes in IP rules in the early 1980s in the US allowed universities to patent and transfer technologies to pharmaceutical companies and biotechnology firms. In these transactions, IP is the major currency for the transfer of innovative products from the inventor (the university), to the developer (often a small biotechnology firm), and finally to the manufacturer and marketer (often a large pharmaceutical firm). Public-private partnerships such as the International AIDS Vaccine Initiative (IAVI), the Medicines for Malaria Venture (MMV), and the Global Alliance for TB Drug Development have drawn from these experiences and have developed their own analogous strategies for transferring technology, processes, and products from the rich countries to the developing world.

The Hinxton meeting was held at a time when international debate on trade and development had brought concerns about intellectual property rights and health to center stage. A special contribution of the meeting was its emphasis on the interrelatedness of access and R&D and the importance of not focusing on one goal to the exclusion of the other. The public health challenges are large and the opportunities are many, but the polarizing nature of the current debate diverts precious energy away from concerted action. Participants at the meeting urge all key players—government officials, international organizations, foundations, the private sector, and the activist community—to strive for unity of purpose and a spirit of cooperation in making the advances in biomedical science and biotechnology available to all.

Section I Introduction

Health disparities between populations of rich and poor countries are very wide. Average life expectancy at birth in the poorest countries is half that of the richest. In many countries, the mortality rate of children under 5 years is over 20 percent, whereas in the richest countries it is around 0.6 percent. Furthermore, the problem is worsening. The AIDS epidemic has taken a serious toll in sub-Saharan Africa, reducing average life expectancy by over 10 years in some countries. Multi-drug resistance is increasing in many parts of the developing world—threatening to undermine the effectiveness of the current artillery of drugs used to combat tuberculosis and malaria. As the rich countries benefit from rapidly advancing technologies in health, poor countries of the world are falling behind.

The problem of health disparities has both a current and a future dimension. On the one hand, the international health community desires to promote affordable access to existing drugs and vaccines for the people who need them. On the other, it wants to stimulate the development of new drugs and vaccines targeted specifically at the diseases of the poor. Neither represents a comprehensive response to the problem of health disparities, but both objectives are important and must be tackled simultaneously.

The primary focus of this report is intellectual property rights protection—the critical element that gives rise to the interrelationship between access and incentives for research and development (R&D). The spotlight is on whether current systems of patent protection, both domestic and international, strike the correct balance between creating incentives for drug discovery and development and ensuring access to existing and patentable products.

To develop a better understanding of linkages between intellectual property rights and public health, the Wellcome Trust, the Commission for Macroeconomics and Health, and the Institute for Global Health convened a meeting entitled "Intellectual Property Rights and Global Health: Challenges for Access and R&D." The meeting was held on December 7–9, 2000 at the Wellcome Trust Genome Campus at Hinxton Hall, Cambridgeshire, UK. Representatives from all the major stakeholders attended: the research-based and generics pharmaceutical and biotechnology industries of the high- and middle-income countries, governments, academics, public-private partnerships, the US National Institutes of Health, the Wellcome Trust, the World Trade Organization (WTO), and nongovernmental organizations.

The Hinxton meeting was held at a time when international debates on trade and development had brought concerns about intellectual property rights and health to center stage. Some of the questions raised at the meeting were left unanswered, either because the facts were not yet in or because consensus on a subject of such complexity remained elusive. This report draws on the discussions at the Hinxton meeting but supplements them with new information that emerged rapidly in its wake. It is important to note that the first jointly sponsored meeting of the World Trade Organization (WTO) and the World Health Organization (WHO), held in April 2001, helped to clarify some of the common misperceptions about what the TRIPS (Trade-Related Aspects of Intellectual Property Rights) Agreement—negotiated as part of the Uruguay Round of GATT—would mean for health.

This report is not a consensus statement in the strictest sense because of the new information and analysis it contains. However, certain themes emerged at the meeting that helped push the debate forward, and these themes are highlighted here. Participants at the meeting were generally sympathetic to the argument that protection of pharmaceutical innovation in the form of patent rights is required to stimulate private sector investments in R&D. But they were not in complete agreement about how far these patent rights should be extended and whether intellectual property (IP) is the appropriate tool for addressing the larger problem of incentives that skew scarce investment resources toward the diseases of the rich.

Thus, the discussion at the meeting shifted toward the practical. The vast majority of the Hinxton group consisted of academics, legal experts, and health policy

practitioners. These participants tended to focus on public-private initiatives that attempt to use intellectual property as a tool to simultaneously improve access and incentivize R&D without compromising one goal for the other. Their focus was not on "strong" versus "weak" patent systems but on creative applications of intellectual property in support of public health objectives.

The next section provides a brief overview of the TRIPS Agreement and the events that gave rise to it. Section III discusses linkages between intellectual property and R&D from the perspective of pharmaceutical and biotechnology firms, and reviews the potential impact of TRIPS on levels of investment in the neglected diseases of the poor. Section IV examines linkages between intellectual property rights and access and reviews arguments concerning a pricing strategy that purports to provide a solution for access without compromising R&D investments. Section V discusses a range of new initiatives that favor the use of intellectual property as a tool for addressing these issues, and Section VI presents the participants' conclusions.

Section II The TRIPS Agreement

TRIPS is one of the agreements reached at the conclusion of the 1986–1994 Uruguay Round of the GATT Multilateral Trade Negotiations. It is part of a package of agreements that countries sign up to when they join the WTO. TRIPS came into force on January 1, 1995, but the transition periods for its implementation are staggered for countries at different levels of economic development.

Before TRIPS, there were two main multilateral agreements on international protection of intellectual property rights—the Paris Convention for the Protection of Industrial Property of 1883 (on trademarks, patents, etc.) and the Berne Convention of 1886 (on copyrights). By the 1980s, US, Japanese, and European firms had begun to view these agreements as inadequate and out-of-date in light of changes in the global economy that made their national economies more dependent on the production of knowledge. In recent years, middle-income countries such as Brazil and South Korea and large, low-income countries such as India have become increasingly competitive in knowledge-based industries—including pharmaceuticals and biotechnology.

The fact that many countries in the developing world did not recognize patents on products—or, in some cases, on processes—was a major problem for the global pharmaceutical industry. The research-oriented pharmaceutical firms were concerned that they would lose their export markets to firms that specialize in "reverse engineering"—copying products under patent in the developed world and selling them at discounted prices in local and regional markets in the developing world.

Hence, the pharmaceutical industry joined with other knowledge-based industries in the US, Europe, and Japan to support the inclusion of intellectual property protection in the Uruguay Round of the GATT negotiations. Lengthy negotiations among WTO members resulted in the TRIPS Agreement, which requires signatory countries of the WTO to recognize and protect both process and product innovations in all fields of technology (Siebeck 1990).[1]

For pharmaceuticals, as well as other fields of technology, patent protection under TRIPS extends for 20 years.[2] Although TRIPS sets the minimum standards for patent protection globally, the impact is felt differently by developed and developing countries. Becoming TRIPS-compliant implied few major legal adjustments for the developed countries of Europe, North America, and parts of Asia. By contrast, many countries in the developing world offered more limited patent protection and were faced with the need to make more extensive changes.[3] To accommodate this difference, the transition periods for implementation were staggered for countries at different levels of economic development. Also, the World Intellectual Property Organization (WIPO) agreed to work with the WTO to facilitate the implementation of the TRIPS Agreement. This included offering technical assistance for patent system reform to countries seeking to become TRIPS-compliant.

Under TRIPS, patent rights are not absolute and are subject to limitations and exceptions. Countries can allow third parties to use a patented invention for research purposes if the aim is to understand the invention more fully as a basis for advancing science and technology. In addition, countries may allow generic companies to develop and seek marketing approval for copies of the patented product — prior to expiry and without permission of the patent owner — to prepare for market entry when the patent expires. This provision is sometimes called the "regulatory exception" or the "Bolar" provision (Article 30) (see box below).

Research Exception and the "Bolar" Provision

Many countries allow third parties to use a patented invention for research purposes where the aim is to understand more fully the invention as a basis for advancing science and technology.

In addition, some countries allow manufacturers of generic drugs to use the patented invention to obtain marketing approval—for example, from public health authorities—without the patent owner's approval and before the patent protection expires. The generic producers can then market their versions as soon as the patent expires. This provision is sometimes called the "regulatory exception" or "Bolar" provision (Article 8).

This has been upheld as conforming with the TRIPS Agreement in a WTO dispute ruling. In its report adopted on 7 April 2000, a WTO dispute settlement panel said Canadian law conforms with the TRIPS Agreement in allowing manufacturers to do this. (The case was titled "Canada—Patent Protection for Pharmaceutical Products").

Source: Extracted from WTO Fact Sheet, "TRIPS and Pharmaceutical Patents," April 2001.

Of particular importance to health care (the exceptions listed above apply across all fields of technology indiscriminately), WTO signatories under TRIPS can refuse to grant patent protection for three types of inventions: those in which commercial exploitation must be prevented to protect health or human, animal, or plant life; diagnostic, therapeutic, and surgical methods for treating humans or animals; and certain plant and animal inventions (Articles 27.2, 27.3(a), and 27.3(b), respectively).

Other possible exceptions under TRIPS (addressed in Section IV) have special relevance for the ability of developing countries to obtain patented drugs at affordable prices. These exceptions relate to the ability of countries to bypass patent rights in order to produce or import patented products predominantly for domestic use (compulsory licensing) or to import drugs that the patent owner has sold elsewhere at lower prices (parallel importing).

Section III Intellectual Property Rights and Drug Discovery and Development

Existing technologies for the prevention, diagnosis, and treatment of many of the diseases of the poor are either inadequate or nonexistent. If new medicines are not developed, the health gap between rich and poor will surely increase over time. Yet present levels of R&D investments targeted at the neglected diseases are low.

The Global Forum reports that of the US $50–$60 billion spent globally on health research each year, only 10 percent is directed toward developing treatment or finding cures for 90 percent of the world's population (10/90 Report on Health Research 1999). The potential profitability of developing-country markets is small relative to that of developed-country markets. In 2000, developing-country markets accounted for only 20 percent of global pharmaceutical sales — and sub-Saharan Africa for less than one percent (Watal 2001).

Both during and after the negotiations of the TRIPS Agreement, attention focused on the potential impact of TRIPS on R&D incentives in the area of the neglected diseases. Industry argued that strengthening patent protection would stimulate research in areas of concern to developing countries, on the assumption that local industry in those countries would have an incentive to focus on "their" diseases (Lanjouw 1998). Critics responded that strengthening patent protection would stamp out local industry. It is important to distinguish between two separate debates that underlie these distinct positions. One concerns the potential impact of TRIPS on incentives for private industry—in developed or developing countries—to invest in the neglected diseases. The other concerns the impact of TRIPS on existing pharmaceutical industries in developing countries.[4] Participants at the Hinxton meeting sought to disentangle these two issues and to focus particularly on the first—the aspects of intellectual property that affect levels of R&D investment directed toward products for the neglected diseases.

THE IMPORTANCE OF PATENT PROTECTION TO INDUSTRY

The message from research-based pharmaceutical and biotechnology companies is clear: without patent protection, there will be no R&D. Two features of pharmaceutical research and development explain why. First, the sunk costs of R&D are high, averaging $300–$600 million per new product, and amounting to more than 30 percent of the total cost of developing, producing, and marketing the typical product (the estimate includes the cost of failures and the opportunity cost of funds during the R&D process) (Kettler 1999). Second, the marginal cost of pharmaceutical production is often low.

Although the R&D process is lengthy and risky, most pharmaceutical products are relatively cheap to produce once they have been discovered and developed. This feature is what permits generic firms to launch products at prices well below the cost of a branded product, following expiration of the patent. Without patent protection and the secured period of market exclusivity, generic products would enter the market immediately following product launch, and force prices down to marginal cost. Since marginal costs do not cover the fixed costs of R&D, the likely result would be a decrease in R&D and hence a decrease in new products brought to market by the research-based industry.

Protection of intellectual property is similarly important to biotechnology and is a vital component of the start-up company's essential asset base. Venture capitalists, potential alliance partners, and the stock market all evaluate companies according to their IP profiles, among other things, in the critical decision on whether to fund the risky R&D that may eventually lead to product launch (and earnings income based on actual sales). In addition, IP plays an important role in commercializing the research discoveries of biotechnology firms. For example, firms can transfer patented technologies to industry partners via licenses. Companies can choose to "out-license" a patent in a field outside its core focus, thereby gaining revenues and potential royalties should the recipient turn the patent into a marketable product.

Universities also seek industry partners to identify market applications for their research. Changes in rights and laws in the US and, more recently, in some European countries have enabled universities to either grant exclusive licenses or transfer technologies to companies will-

ing to risk investment in an unproven application and bring the product to market (Table 1 shows relevant US legislation). The opportunity to patent university research induces these companies and venture capitalists to invest in early-stage university technology. The potential for mutual benefit is large. Table 2 lists the top five royalty-earning institutions in the US in 1998.

Table 1. US Technology Transfer Legislation

Bayh-Dole Act (1980)
• Granted rights to universities and small business to patent inventions developed with public funds • Authorized federal agencies to patent and license their inventions
Stevenson-Wydler Technology Innovation Act (1980)
• Made clear that technology transfer is a mission of all federal labs • Executive Order 12591 (1987) required that heads of executive departments and agencies encourage technology transfer
Federal Technology Transfer Act (1986) and Subsequent Amendments
• Allowed government scientists to retain and share royalty fees with the inventors and provides mechanism for Cooperative Research and Development Agreements (CRADAs)

Source: Presentation by Gerald Keusch, Director, Fogarty International Center (US NIH), Hinxton Meeting, December 7–9, 2000.

Table 2. Royalty Earnings from Patents and Licenses, 1998

Institution	Income (millions)	New patent applications	Licenses executed
University of California	73	633	177
Columbia University	62	85	112
Florida State University	46	22	7
Stanford University	43	234	118
US National Institutes of Health	40	132	215

Source: Presentation by Gerald Keusch, Director, Fogarty International Center (US NIH), Hinxton Meeting, December 7–9, 2000.

Although these examples provide an indication of how and why IP is critical to R&D, it is also true that excessive patenting can sometimes act as a barrier to innovation, slowing down the movement of ideas to market and reducing potential returns from successful products. Because of the large number of technological processes required as inputs to product development, individual companies are simply not able to keep all processes in-house. Acquiring the necessary licenses and sorting out the state of play of patents filed in order to obtain "freedom to operate" without infringing on rights held by others is expensive and time consuming for an individual company.

For example, pharmaceutical firms must often negotiate with multiple parties (universities, consortia of institutions, nongovernmental institutions, corporations, and individuals) to gain access to the often overlapping and interwoven intellectual property rights needed to develop a single product. When multiple parties are involved in developing a final product, they end up sharing the returns. The company launching the final product pays royalties to the multiple partners that have contributed to it—a process referred to as "royalty stacking."

Arguably, biotechnology firms have benefited the most from existing patent standards, since it is under these standards that the patenting of platform technologies is permitted. But royalty stacking also presents a problem for biotechnology firms. As Table 3 indicates, the development of a malaria vaccine may require the collaboration of as many as seventeen parties.

Table 3. Hypothetical Example: Parties Contributing to Development of a Vaccine for Blood-Stage Malaria

Multi-component antigens	2–10 parties
Vaccine vector	1–2 parties
Delivery formulation/adjuvant	0–2 parties
Manufacturing process	0–2 parties
Delivery modality	0–1 parties
Total	3–17 parties

Source: Presentation by Russell Howard, CEO, Maxygen, Inc., Hinxton Meeting, December 7–9, 2000.

Although a technical review of patentability and the implications of excessive patenting was beyond the scope of the meeting, several points were raised. First, there has been growing concern among legal and biotechnology experts that current patent standards have failed to adapt to the challenges of the genomic age and are inappropriate for biomedical science. In the opinion of some scholars, excessive patenting may result in a breakdown of the implicit contract, since the objective of the patent system is to reward innovation, not to "diminish the amount of usable information in the public domain" (Barton 2000b). And although TRIPS is not responsible for the emergence of this pattern of patenting, it may reinforce existing inefficiencies unless appropriate action is taken to eliminate them (Correa 2000). The Commission on Intellectual Property Rights convened in early 2001 by the UK government will study this issue and its potential impact on developing countries.[5]

THE IMPACT OF STRENGTHENING PATENT PROTECTION IN DEVELOPING COUNTRIES

Although the adoptions of TRIPS is used as a standard benchmark for when developing countries began strengthening their patent systems, many countries had already started the process of patent reform before the closure of the Uruguay Round of negotiations. Chile, Indonesia, Mexico, South Korea, and Thailand, as well as the Andean countries of Bolivia, Colombia, Ecuador, Peru, and Venezuela all reformed their patent laws to cover pharmaceutical products prior to the TRIPS accord, often in response to bilateral pressure from the US. By the time that TRIPS came into force, fewer than 20 developing and least-developed members of the WTO excluded pharmaceutical products from patent protection. However, the list of WTO members that did not grant pharmaceutical products patent protection included a number of the key developing-world pharmaceutical producers, including Argentina, Brazil, Cuba, Egypt, and India[6] (Watal 2001).

In recognition that some countries would need time to adjust their patent systems to become TRIPS-compliant and that the burden of adjustment would fall heavily on the resource-poor governments of the developing world, TRIPS sets out somewhat complicated transition provisions. The time periods differ according to the type of obligation in question and the stage of development of the country concerned. For the pharmaceutical industry in particular, the obligations can be divided into three categories:

- Provisions relating to the introduction of product patent protection for pharmaceuticals for those developing-country members of the WTO not yet granting it.
- Provisions regarding the application of TRIPS rules on process patents in those countries not yet granting them.
- Provisions regarding the application of all TRIPS patent rules in other countries.

With respect to process patent protection—as well as product patent protection in countries already making such protection available—developing-country members had until January 1, 2000 and least-developed country members until January 1, 2006 to meet the obligations in question (with the possibility of an extension in the case of least-developed countries). At that time, the rules of TRIPS

WHAT DO DEVELOPING COUNTRIES GAIN BY SIGNING UP TO THE TRIPS AGREEMENT AND ADOPTING ITS PROVISIONS?

This question touches on much broader issues than pharmaceuticals, since it concerns all areas of economic activity and other categories of intellectual property rights, as well as the broader stake that countries have in the Uruguay Round negotiations and the health of the multilateral trading system. In the area of pharmaceuticals, the answer to the question obviously varies by country and depends in part on the current state of development of the country's pharmaceutical industry. A 1991 UNESCO study found that among the low- and middle-income countries, only Argentina, China, India, Israel, Mexico, and South Korea had industries with innovative capabilities. Eight others, including Brazil, Cuba, Egypt, and Indonesia could produce therapeutic ingredients and finished products that were competitive in regional export

Table 4. The "Standard" of the Pharmaceutical Industry, by Country

Sophisticated Pharmaceutical Industry and Research Base	Innovative Capabilities	Reproductive Capabilities — Therapeutic Ingredients and Finished Products	Reproductive Capabilities Finished Products Only	No Pharmaceutical Industry
			87 countries including:	59 countries including:
Belgium[a]	**Argentina**	Bahamas	Algeria	Botswana
France	**Australia**	**Bolivia**	**Bangladesh**[b]	Burundi
Germany	**Austria**	Brazil	Belize	Central African Republic
Italy	**Canada**	Bulgaria	Cambodia	Chad
Japan	**China**	Cuba	Chile	Congo
Netherlands	**Denmark**	**f. Czechoslovakia**[c]	Columbia	Gabon
Sweden	**Finland**	Egypt	**Costa Rica**	Guam
Switzerland	**Hungary**	**Indonesia**	**Dominican Republic**	Guinea
United Kingdom	**India**	**Norway**	**Ecuador**	Laos
United States	**Ireland**	**Poland**	**El Salvador**	Martinique
	Israel	Puerto Rico	Ethiopia	Nauru
	Mexico	Romania	Gambia	Oman
	Portugal	**Turkey**	**Greece**	Rwanda
	Korea		**Guatemala**	Samoa
	Spain		**Honduras**	Senegal
	f. USSR[c]		**Hong Kong**	Suriname
	f. Yugoslavia[c]		**Kenya**	Togo
			Lebanon	
			Malaysia	
			Morocco	
			New Zealand	
			Nicaragua	
			Peru	
			Philippines	
			Singapore	
			Somalia	
			South Africa	
			Taiwan	
			Thailand	
			Uruguay	
			Venezuela	
			Zimbabwe	

Notes: [a] Countries in bold are members of the IFPMA as of 2000.
[b] Bangladesh is the only country that is both a member of the IFPMA and one of the 48 UN designated "least developed countries."
[c] f. = former.

Source: Ballance et al, 1992, www.wto.org;www.ifpma.org.

markets. A further 87 countries could produce some finished products using imported compounds. Fifty-nine countries had no industry at all and were totally reliant on imports to meet their pharmaceutical requirements (see Table 4) (Ballance et al, 1992).

Some would argue that in order to realize new R&D opportunities from changes in their patent law, countries must already have built up the infrastructure to innovate. This applies to the handful of countries in column 2 of Table 4 that have innovative capabilities, plus a few others—notably, Brazil and perhaps Cuba—that will have graduated from column 3 to column 2 in the intervening years since the completion of the UNESCO study.

India's experience. India is a good example of a country whose companies, as of 2005 and the implementation of TRIPS patent rules, should be ready to compete on the basis of innovation. In 1970, the Indian government implemented the Indian Patent Act as part of a wider set of policies to develop a "self-reliant" pharmaceutical industry. Under the Act's provisions, preexisting product patent protection rules were eliminated and process patents were reduced to seven years. In many ways, these measures have successfully achieved their goal. As of 1999, an estimated 8,000 - 20,000 mostly small, Indian-owned companies were in existence, employing more than 2.86 million people (Lanjouw 1998; Indian Federation of Drug Manufacturers' Association (IDMA) 2001). Turnover in formulation production increased 80-fold between 1965 and 1997, and bulk drug production increased 145-fold over the same period. The growth and geographic breadth of India's export market indicate that global quality standards have been achieved in a number of product areas.

To realize this rapid growth under a weak patent regime, the majority of India's pharmaceutical companies have pursued a reverse-engineering strategy. They imitate and produce drugs protected by patents in other countries and sell them in India and international markets where patents are not recognized. Also, Indian companies compete in international generics markets after patents have expired.

As India moves to adopt the TRIPS Agreement, a number of the country's leading companies are already shifting away from the reverse engineering of existing drugs and toward investments in the discovery and development of new molecules. The Indian government is aware that the development of a drug-discovery business depends on more than just changes in the patent laws. It is taking action to build up other innovation-supporting institutions such as the public research base; the pool of skilled scientists, engineers, and technicians; the price and tax regimes; and the capital funds available for entrepreneurial endeavors.

The Cuban example. Cuba provides an interesting contrast. For nearly two decades, the Cuban government has supported a series of initiatives designed to exploit the advantages of biotechnology in the health care sector. As with India, the development of the industry was part of a larger strategy to decrease dependence on foreign markets for health products, in the expectation that they could be produced more cheaply at home. In addition to meeting domestic demand, the Cuban government's goal was to export these products to countries of the former Eastern Bloc and nonaligned countries of the developing world.

Early Cuban successes can be partly attributed to a strategy of copying patented processes and products, but carefully planned and coordinated R&D investments and the existence of a highly educated scientific workforce with expertise in biochemistry and microbiology were also key. These resources have been critical for the industry's survival because it has had to mature quickly to deal with the recent challenges posed, first, by the economic crisis precipitated by the collapse of the Soviet Union and, second, by Cuba's signing of the TRIPS Agreement in 1995. Although Cuba has a strong foothold in some markets of Latin America and elsewhere in the developing world—particularly for the meningitis B and hepatitis B vaccines—its position will be increasingly challenged as the larger pharmaceutical firms shift their attention to growing markets in the South.

Cuba's future in R&D activity will hinge partly on how successfully it has developed a self-sustaining innovative capacity. By implementing TRIPS, Cuban firms will no longer be able to profit from the sale of domestically produced copies of patented products abroad.

Given its particular geopolitical history, Cuba is by no means representative of the majority of low-income countries, which have either limited production capacity to produce finished products or no capacity at all. Their options for purchasing copies of patented drugs from suppliers such as Cuba and India will be more limited in the post-TRIPS period. For these countries, which consume health care products produced overseas by foreign firms, the issues of access are immediate and problematic—whereas the future gains to be had from R&D investments today are felt only remotely.

WILL DEVELOPING COUNTRIES BE BETTER PLACED TO ADDRESS EXISTING R&D GAPS IN NEGLECTED DISEASES UNDER THE NEW IP REGIME?

Participants at the Hinxton meeting were particularly interested in this question. Although more research is needed, there is no concrete evidence so far to suggest that companies in Brazil, India, or elsewhere will have any more interest in investing in neglected diseases than do global private companies in the US, Europe, or Japan. The expectation that they do is based on the assumption that local companies could discover and develop drugs at a fraction of the costs of global players and thus make a "neglected disease" strategy profitable, despite the low purchasing power of the patients. Volume sales of low-priced products could pay off if the R&D costs are sufficiently low.

The basis for this proposition seems weak for a number of reasons. First, to realize these optimistic cost savings, significant investments in drug discovery and development are needed. Such cost savings also depend on a steep and rapid learning curve for companies that, with few exceptions, have until now done little or no R&D of the type required to discover, develop, and market new products. Second, even if companies were capable of realizing such low costs, money-making opportunities from diseases of the rich will be many times greater than those from neglected diseases, unless we assume significant differences in the cost structures of R&D for the two types of diseases (Kettler and Modi 2001). Not surprisingly, Cipla and Ranbaxy, two of the largest research-based pharmaceutical firms in India, have targeted global markets by focusing their research on conditions of concern to the wealthy and aged, including cardiovascular disease, diabetes, and cancer. In fact, a 1999 survey of Indian firms indicated that only 16 percent of R&D expenditures were targeted at tropical diseases (Lanjouw and Cockburn 2000).

Thus, although protection of intellectual property rights is a necessary condition for innovative R&D, it is certainly not sufficient for promoting R&D in the area of neglected diseases. It is clear, however, that the absence of IP protection would be a distinct disincentive for private-sector R&D investments. But for MSF (Médicins Sans Frontiéres—Doctors Without Borders) and other groups that downplay the importance of private-sector investments for the most neglected of the neglected diseases, this defense of IP seems unjustified. Instead, they support massive public-sector investments in these areas and are skeptical about why strong IP protection should matter to these public research ventures.

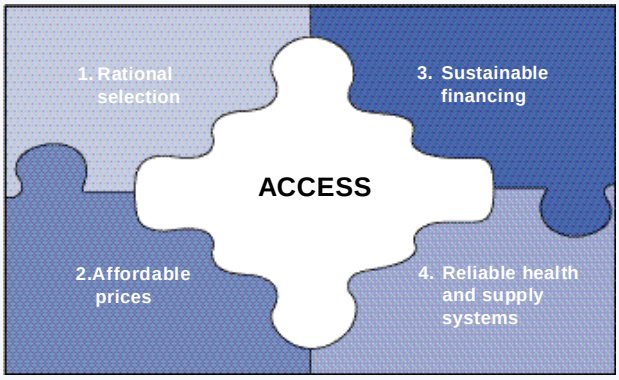
Participants at the Hinxton meeting did not resolve this disagreement, but they worked around it. Many were eager to discuss access and R&D incentives as part of a unified package, and so the spotlight shifted toward the practicalities of using intellectual property rights as a tool to achieve both goals.

Section IV Intellectual Property Rights and Access

Only a small percentage of the developing-world countries are producers of pharmaceuticals, but all countries are consumers. For many poor countries, gaining access to affordable drugs and vaccines is a critical challenge.

The UN Industrial Development Organization (UNIDO) has calculated that approximately one-third of the developing countries import 100 percent of the medicines they consume. Nearly two-thirds import more than half (this estimate is based on value rather than quantity terms) (Scherer and Watal 2001). While many other factors besides price may impede access to affordable drugs — including rational selection, sustainable and adequate financing, and reliable health care and supply systems — price is an important factor.[8] Figure 1 provides a graphic representation of the key components of access as described by the Essential Drugs and Medicines Policy Department (World Health Organization).

Figure 1: Key Components of Access



Source: Essential Drugs and Medicines Policy Department, World Health Organization

Price is the factor relevant to access that is commonly linked to patent protection. Whether a product is on- or off-patent clearly affects the product's price within its own lifecycle. At the heart of the debate on intellectual property rights and price is whether countries delay the entry of cheap, generic copies into their markets by adopting the TRIPS Agreement, thereby denying their populations access to affordable patented drugs in the near term. Hence, this section focuses on the effect of TRIPS on prices, as mediated by the patent system.

TRIPS, PRICES, AND AFFORDABILITY

Drug Prices in Developing Countries That Become TRIPS-Compliant

Existing prices. Prices of existing products are not expected to change significantly. The reason is that any product patented before 1995 is not covered by TRIPS for those countries that did not previously provide product patent protection for pharmaceuticals. (However, a number of these countries have extended pipeline protection to some of these products.) Of the 300 drugs on WHO's Essential Drug List (EDL), fewer than 20 are currently on-patent. Since affordability is an important criterion in selecting products for the EDL, some patented drugs that are essential will not be listed. However, the fact that over 95 percent of medicines on the list are currently off-patent is noteworthy. And the issue of patentability is further placed in perspective by the fact that over 50 percent of the total population of Africa and Asia lacks access even to these essential medicines, according to WHO statistics.

Patentable products. While off-patent products will not be affected, the effect of TRIPS on the patentable segment of the pharmaceutical market is likely to be significant. In other words, implementation of TRIPS will affect the soon-to-be-launched and future products rather than existing ones. In those countries that did not previously grant product protection for pharmaceuticals, TRIPS will delay the date of entry for generic versions of products patented after 1994. To some extent, it will also have this effect in other countries where the term of protection was previously below the TRIPS minimum of 20 years. Evidence that prices may be expected to increase under TRIPS can be extrapolated from studies showing that average pharmaceutical prices fall sharply when generic substitutes enter the market following patent expiry.

However, the question of how large an effect patent introduction will have on price is much more difficult to answer. As Scherer and Watal (2001) point out, a reasonable measure would be to compare the price index for a basket of nonpatented goods with the price index for an equivalent basket of patented products, but it is difficult

to include all the controls required to do so. Some studies have estimated the impact to be very large—on the order of 200 percent—but others have indicated a smaller effect, in the range of 30 to 60 percent (Watal 2001). It is important to note that these estimates assume that patent rights will be fully applied and do not take into account the flexibilities afforded under the TRIPS Agreement—for example, in the areas of compulsory licensing, parallel imports, and price controls. Nonetheless, although the estimates are wide-ranging, it is safe to assume that the potential impact of TRIPS will be to raise the prices of patented products, if other policies (including, for example, differential pricing—see the next section) are not adopted.

Consistent with the discussion in the previous subsection, the countries most affected by TRIPS will include the middle-income and large, low-income countries that have well-developed copycat industries capable of producing for domestic consumption and, in some cases, for export. These copycat industries will have to change their business strategies to compete in generics markets. The small, low-income countries that have typically relied on the importation of copycat substitutes from export-oriented drug suppliers will also be adversely affected.

POSSIBLE FLEXIBILITIES

Certain flexibilities under TRIPS may provide recourse for countries seeking access to affordable products.

Compulsory licensing. TRIPS permits WTO members to authorize use by third parties (compulsory licenses) or use for public noncommercial purposes (e.g., government use) without authorization of the patent owner (Article 31) under certain conditions. Governments may undertake to adopt compulsory licensing if a number of conditions are met. Among these is the condition that they first seek to obtain a voluntary license and, failing that, they provide adequate compensation to the patent owner for the compulsory license. Applicants need not attempt to secure voluntary licenses in cases of "national emergencies," "other circumstances of extreme urgency," or for public, noncommercial use of the patent (Article 31[b]).

The TRIPS Agreement allows countries to give compulsory licenses not only for domestic production but also for importation—for example, for the importation of products produced either in a country that does not provide patent protection or in a country that produces under a compulsory license. One potential constraint on this source of drug supplies for developing countries is that TRIPS requires that the use of compulsory licensing be "predominantly" for the supply of the domestic market.

Parallel imports. While not explicitly permitted under TRIPS, parallel imports are permitted de facto. The legal principle here is "exhaustion"— i.e., patent holders relinquish all rights over how a product may be used (traded or re-sold) once it has been sold to an initial purchaser. TRIPS clearly states that none of its provisions can be used to address the issue of exhaustion of intellectual property rights in a WTO dispute (Article 6).[9]

Although these options are available to countries under TRIPS, they are far from ideal solutions to the complicated problem of gaining access to affordable drugs, diagnostics, and vaccines. Legal wrangling over compulsory licensing is likely to be costly, and long licensing delays will work strongly to the disadvantage of countries seeking to obtain a license. The process of reaching agreement on appropriate royalty payments may also be difficult. Finally, parallel importing itself does not appear to be optimal from a long-term perspective. Economic theory suggests that prices will tend to converge to a single global price if parallel importing becomes widespread. While rich countries may ultimately pay less for pharmaceuticals than they would have in a world without parallel imports, poor countries will pay more as prices converge across all markets (Danzon 1998). Further, a single uniform price for all developing countries, irrespective of income levels, may work to the disadvantage of the poorest countries.

Participants at the meeting emphasized that better, more long-term, and stable solutions are needed.[10] The next subsection explores a pricing solution that aims to resolve the problem of access while at the same time enabling firms to recoup R&D investments.

TIERED PRICING ARRANGEMENTS—AN ALTERNATIVE PATH?[11]

In an ideal world, countries would contribute what they can afford to the total costs and prices would be inversely related to the consumers' ability to pay. The "global joint costs"—that is, the fixed costs of pharmaceutical R&D that are the same regardless of the number of purchasers of the final product (Danzon 1998)—benefit all consumers and therefore most optimally will be shared by all. The economic theory of efficient pricing known as "Ramsey pricing" supports the practice of charging different prices to different consumers to cover these costs in addition to the baseline marginal costs (i.e., the baseline cost of production, excluding overhead).

By extrapolation, some economists have argued that an optimal pricing scheme for pharmaceutical products under patent will be one in which all countries contribute to the joint costs of R&D, but at different levels, or tiers, depending on their GDP or some other equivalent measure of ability to pay. This would require that wealthy countries bear a disproportionate amount of the R&D costs of the product in question. Poor countries would contribute only partially or not at all to the cost of R&D. However, payments in these countries would cover the marginal cost of the products they consume. The sum of the difference between the price paid and the marginal cost to each country (or segment of the population) would have to cover the joint fixed costs of R&D. The result: cheaper prices can be made available to poor countries without negatively affecting the R&D incentives of firms. This is what is generally referred to as "differential pricing." Differential pricing should appeal to many stakeholders, with a few important caveats.

Industry. Pharmaceutical firms should find differential pricing appealing because it would increase their sales to markets that have been previously closed to them. However, three concerns could reduce its appeal:

- The low, differentiated price to developing-country markets could be used in setting reference prices in the developed markets.
- The cheaper products made available to developing-country markets could find their way back to markets in the US, Europe, and Japan.
- The cheaper products could also benefit the affluent minority within developing-country markets.

A variety of solutions have been proposed for the second and the third problems, including modifying the packaging and marketing arrangements for the lower priced products. In addition, Danzon (forthcoming) argues that differential pricing is practical wherever different insurance plans for the wealthy and poor contribute to market segmentation.

Public health practitioners. Differential pricing also appeals to those stakeholders with a strong public health mission. However, their concern is how to recognize the true marginal costs of production in the absence of generic production and the full knowledge of industry's R&D costs.[12] It will be necessary for countries to explore effective means of negotiating on the basis of price without having complete information about the true marginal costs of production.

Finally, a potential obstacle to full implementation of a differential pricing model is that many of the world's poor would still be unable to afford the drugs they need—even at close to marginal cost. Hence, increased levels of financing from international sources will be a critical factor in the successful application of differential pricing.

Implementation. Questions have been raised concerning how to implement differential pricing on a large scale. The appropriate institutional vehicle(s) must be identified. A great deal of work will need to be done to identify all of the disparate activities that must come together to turn differential pricing from a good proposal into a viable policy option. These include preventing a backwash of cheap products from developing countries to developed ones and preventing the use of cheap prices offered to poor countries as reference prices for government purchases of drugs in rich-country markets. There are existing proposals for addressing each of these points, so none should be considered obstacles for moving discussions forward (Otten 2001).

Finally, it is important to remember that although differential pricing provides an approach to improving access that does not compromise R&D goals, it also does not directly address the problem of incentivizing R&D in particular areas of concern for poor people in developing countries. In fact, differential pricing only matters when there is an overlap between rich and poor markets for drugs. For the most neglected of the neglected diseases—the tropical diseases affecting predominately the poor in poor countries—it offers no solution. Differential pricing is only one component of a broader package of initiatives to address the incentive problem.

Section V Using Intellectual Property Rights Creatively

Access and R&D are inextricably bound together. A successful approach to one requires that it not negatively impinge upon the other. Hence, we need innovative approaches that work within an agreed-upon intellectual property framework, balancing both investment incentives and public health concerns regarding access.

In each innovative approach explored here, a concerted effort has been made to use IP as an instrument to achieve the twin objectives of stimulating R&D and improving access to products, drawing on the unique strengths of both the public and private sectors.

THE WELLCOME TRUST

Use of defensive patenting. The Wellcome Trust, the largest medical research charity in the world, has invested US $14 million in the SNP Consortium. This represents approximately one-third of the total costs of collaboration between the Trust, 13 pharmaceutical and technology companies, and leading academic centers. The goal of the SNP Consortium is the creation of a high-quality map of genetic markers in the public domain. The Consortium is a not-for-profit organization that has identified 1.2 million single nucleotide polymorphisms (SNPs is“snips”) in the human genome. Variation in these SNPs is expected to serve as markers for an individual’s propensity to acquire diseases that have a genetic component—e.g., Alzheimer’s, diabetes, and some cancers. Dedicated to making all data publicly available over the Internet, the Consortium’s strategy is to undertake “defensive patenting,” meaning that patents are filed only for the purpose of establishing a priority date. The mapped SNPs data are released to the public domain on a regular basis, at no cost, and no restrictions are placed on researchers (academic or commercial) for their use of the data.

The Wellcome Trust’s involvement in the SNP Consortium is part of a broader web of policy initiatives undertaken by the Trust to ensure that key data, fundamental to medical research, remain in the public domain. The Trust has

UNITED STATES NATIONAL INSTITUTES OF HEALTH: USE OF WHITE KNIGHT PROVISIONS

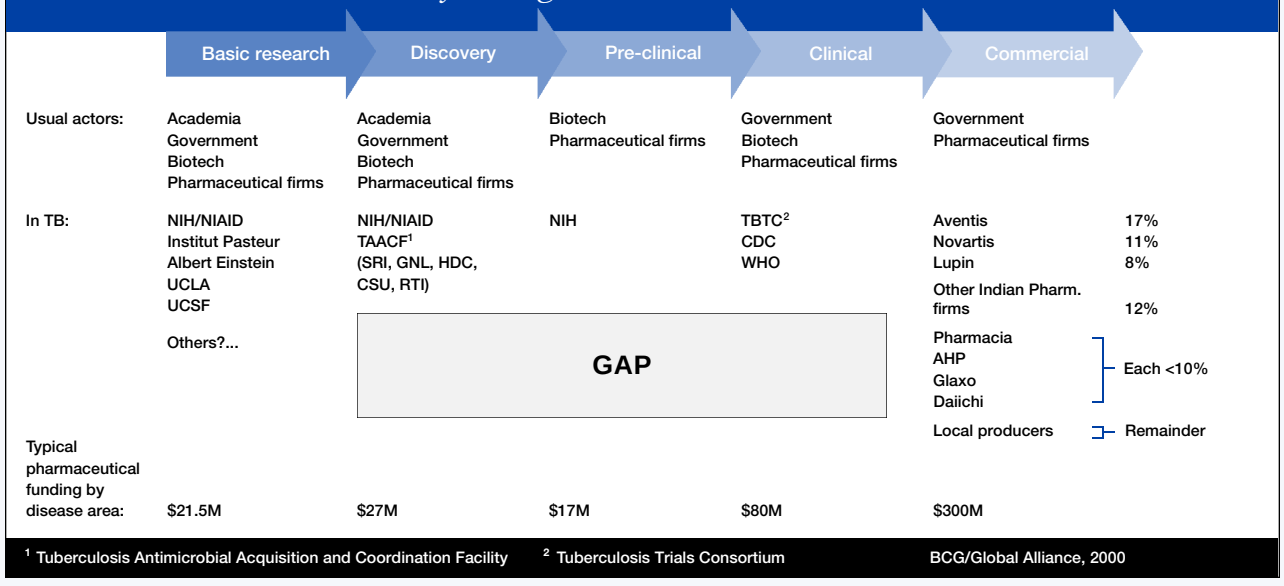
The US National Institutes of Health (NIH) supports basic biomedical research for the health of the public, allocating over 90 percent of its budget to intramural and extramural research. The total research budget for FY2000 was $15.8 billion. Of that amount, $1.8 billion went to intramural research. The Office of Technology Transfer (OTT) was established in the early 1990s. In an effort to foster its public health mission, NIH has introduced the concept of "white knight" provisions—voluntary verbal agreements obliging the recipient of an NIH exclusive license to provide a payback to the community.

These paybacks may take any number of different forms, including an agreement to establish an informational website, to provide the indigent access to the licensed product, or to offer donations to certain communities that may benefit from the product. Since 1996, approximately 80 percent of the NIH exclusive licenses include white knight provisions. However, it is important to note that the white knight provisions apply only to licenses from NIH's intramural research (thus a very small proportion of the NIH investment is awarded in this way).

PUBLIC-PRIVATE PARTNERSHIPS

The importance of public-private partnerships can be demonstrated by a comparison of the partners involved in the R&D process for tuberculosis (TB) compared to a "traditional" disease. The absence of private industry in the pre-clinical and clinical phases is striking. The picture portrayed in Figure 2 is similar for all neglected diseases. The public-private partnerships described here seek to increase the amount of R&D taking place either by attracting more private involvement in specific disease areas or by substituting public actors into stages of the R&D process traditionally dominated by the private sector. The arena of public-private partnerships for neglected products was also discussed extensively at the first Global Health Forum on Creating Global Markets for Neglected Drugs and Vaccines: A Challenge for Public-Private Partnership (Quail Lodge, Carmel, California, February 19-21, 2000).

Figure 2 - *Current Activity along the R & D Value Chain* - Who's Doing What



Source: Presentation by Ariel Pablos-Mendez, Rockefeller Foundation, Hinxton Meeting, December 7-9, 2000.

Changes in the IP rules in the early 1980s in the US allowed universities to patent and transfer technologies to biotechnology and pharmaceutical companies. In these transactions, IP is the major currency for the transfer of innovative products from the inventor (the university), to the developer (often a small biotechnology company), and finally to the manufacturer and marketer (often a large pharmaceutical firm). An analogous model may be useful for stimulating the transfer of technology, processes, and products from the industrialized countries to the developing world. Public-private partnerships set out to use innovative IP arrangements and public funds together to attract private industry involvement in R&D for products for the developing world. This subsection provides a brief snapshot of a few of these arrangements.

The International AIDS Vaccine Initiative (IAVI). IAVI seeks to use public money to support companies or research institutions that develop an HIV vaccine that will benefit populations in the developing world. Its collaborative agreement with AlphaVax serves to illustrate how it is using IP as one of the tools to incentivize R&D in this area.

IAVI sought to develop an HIV vaccine based on AlphaVax's "Replicon" Venezuelan equine encephalitis vector which has been licensed exclusively from the University of North Carolina. In the deal, AlphaVax gained substantial funding, enhanced credibility with funders and potential alliance partners, and ownership of any patents developed under IAVI funding. IAVI has the right to file and own if AlphaVax chooses not to patent. If AlphaVax cannot meet the lowest costs for manufacture, it must license all necessary IP rights to IAVI. AlphaVax also agreed to pay IAVI low royalties on program patents used for products sold to industrialized countries and agreed to forgo all royalties on public-sector sales in developing countries.

This project has yet to realize a product, so it is not yet possible to evaluate the effectiveness of such arrangements. However, IAVI's success in finalizing this type of deal demonstrates the willingness of the some companies to participate, and has clearly stimulated greater R&D investment in HIV vaccines for the developing world.

Medicines for Malaria Venture (MMV). In a similar vein, MMV was established with the goal of obtaining adequate funding to support and manage a portfolio of drug discovery and development leading to the registration and commercialization of one new antimalarial product every five years. MMV's approach is to assume a large portion of the R&D costs and to assist in project management, thereby lowering the cost and risk to firms seeking to commercialize MMV products downstream. Unlike IAVI, MMV will seek patent protection for its financed discoveries and will then license the technologies to the private sector for development and marketing. Royalties from these licensing arrangements will be channeled back into MMV so that it may become partially self-sustainable.

Global Alliance for TB Drug Development. Formed by the Rockefeller Foundation in collaboration with such partners as the Stop TB Initiative, NIH, the Bill and Melinda Gates Foundation, the International Federation of Pharmaceutical Manufacturers Association (IFPMA), and WHO, the Global Alliance is another example of a new initiative that intends to use IP creatively to stimulate R&D activity. The Global Alliance is part of a broader package of policy initiatives designed to curb the worldwide reemergence of TB. Its mission is to accelerate the discovery and development of new, cost-effective TB drugs that will shorten the duration of treatment, improve the treatment of latent TB infection, and overcome the threat of multi-dug-resistant TB. Like IAVI, the Alliance seeks to use public venture capital investments to orchestrate R&D work with commercial and public research institutions. In its business model, the Alliance presents itself as an "incubator"—as distinguished from a grant maker (like the US NIH) or a pharmaceutical company.

The Alliance will maintain a flexible IP approach in negotiating and providing financial and technical support. Regarding IP ownership and control, its options include royalties, march-in rights,[13] non-exclusive licenses,[14] exclusive licenses,[15] ownership for specific applications, ownership in entirety, and any combination of these. The scope of intellectual property rights sought and obtained will vary depending upon such external factors as timing and place in the pipeline, funding needs, and business and other economic factors. In addition to seeking certain intellectual property rights, the Alliance may use other contractual tools—including restrictions on use and expenditure of funds, funding contingent on certain manufacturing or distribution conditions, technology transfer requirements (particularly in the event of a default under a funding agreement), and information disclosure requirements for Alliance purposes (for limited use). In selecting among competing projects, the Alliance will give preference to drug development for which it can hold the majority of intellectual property rights and to joint ventures that involve institutions in TB-endemic countries.

PUBLIC-SECTOR APPROACHES

The examples listed so far start with the premise that important new initiatives to stimulate R&D activity in the area of neglected diseases can be implemented within the existing system of intellectual property rights. However, some groups—MSF and Oxfam in particular—have complained that too much credence is given to the importance of intellectual property in the R&D process. Their argument is that IP protection may be considerably less, or not at all, important for the development of drugs in those disease areas where there is no significant market—e.g., sleeping sickness.

MSF is exploring the possibility of launching an independent, publicly funded, not-for-profit initiative (NfPI) for the development of drugs for the most neglected of the neglected diseases. The mission of the NfPI would be to develop new and affordable medicines for these diseases in collaboration with both the public and private sectors of the developed and developing countries. A potential strategy will be to target "on the shelf" leads—chemical entities in public or private sector compound libraries that may contribute to product development. The expectation of MSF is that the NfPI would obtain nonexclusive licenses to work with these chemical entities.

At the Hinxton meeting, questions were raised about whether a public organization could effectively control and manage the entire R&D pipeline. Industry, in particular, voiced the concern that it would be difficult to fence off the disease areas for which these nonexclusive licenses would be granted.

OTHER INITIATIVES

The Hinxton meeting helped lay the groundwork for the launching of two other new initiatives designed to use IP creatively to support R&D activities in the area of the neglected diseases. Interestingly, both of these new initiatives are supported by the Rockefeller Foundation, which has a long-standing history of supporting research in intellectual property protection in agriculture.

Biotechnology Foundation for Neglected Diseases. This proposed foundation, the brainchild of Russell Howard, CEO of Maxygen, is still in the conceptualization stage. The foundation is to be jointly launched by the Rockefeller Foundation and the Institute for Global Health. Its goal is to channel biotechnology research into neglected diseases of the developing world. In the conceptualized model, a number of biotechnology companies will join in a not-for-profit foundation with financial support from industry, government, and public and private venture funds. The foundation will consist of a management and scientific team that will set disease goals and priorities, identify promising technology, and contract with biotechnology companies to apply specific technologies toward one or more of the priority neglected diseases. These participating companies will retain the IP rights but would cede rights to the foundation for application in agr

Section VI Conclusions

- **Participants at the Hinxton meeting were cautiously optimistic about the role that IP can play in helping to improve global health outcomes.** While recognizing that IP protection may limit the ability of poor countries to obtain access to patented pharmaceutical products at affordable prices, if other policies are not adopted, participants stressed that IP plays a critical role in stimulating private-sector R&D by rewarding innovation. In addition, accelerating drug and vaccine development offers a promising way to improve the health conditions of the poor in the developing world.
- **Participants stressed that IP, although a necessary condition for R&D, was by no means a sufficient condition for stimulating investments in the area of neglected diseases.** Private sector involvement in this area has been limited because the potential profitability of developing-country markets is small relative to that of developed-country markets. Comprehensive approaches to correct the problem are needed, including greater public-sector funding of research, better incentives for private sector investments, and new partnerships between industry and governments to allow for the rapid discovery and development of needed products.
- **Participants emphasized creative strategies and working within the existing system of IP rights to simultaneously improve access to affordable products and stimulate R&D.** Discussions at the meeting focused on the feasibility and desirability of differential pricing—enabling poor countries to purchase patented products at low prices (close to the marginal cost of production) while the rich countries pay more (thus, covering the R&D costs of the product). This was an attractive proposal in the eyes of many participants, although they stressed that it would only apply to pharmaceutical products that are marketed in both the rich and the poor countries.
- **Participants also discussed how IP and licensing arrangements could be better used to link the goals of access and R&D.** This has been the strategy adopted by many of the public foundations and public-private partnerships that were represented at the meeting, including the Global Alliance for TB, IAVI, and MMV. The meeting helped to inspire the development of important new initiatives that will further explore the potential of IP as an instrument to promote public health goals, rather than as an obstacle.

The Hinxton meeting was held at a time when the international debate on trade and development had brought concerns about intellectual property rights and health to center stage. Hence, a special contribution of the meeting was its emphasis on the interrelatedness of access and R&D and the importance of not focusing on one goal to the exclusion of the other. The public health challenges are large and the opportunities are many, but the polarizing nature of current debates diverts precious energy away from concerted action. Participants at the meeting urge all key players, including government officials, international organizations, foundations, the private sector, and the activist community, to strive for unity of purpose and spirit of cooperation in making the advances in biomedical science and biotechnology available to all.

Appendix A

INTELLECTUAL PROPERTY RIGHTS AND GLOBAL HEALTH: CHALLENGES FOR ACCESS AND R&D

Hinxton Hall Conference Centre, Hinxton, Cambridgeshire, UK December 7-9, 2000

List of Participants

Professor John Barton
Stanford Law School
Stanford University
Stanford, CA
USA

Dr. Seth Berkley
International AIDS Vaccine Initiative
New York, NY
USA

Mr. Robert Blackburn
Chiron Corporation
Emeryville, CA
USA

Mr. Richard Blackmore
British Technology Group
London
UK

Professor Martin Bobrow
Wellcome Trust Centre for Molecular Mechanisms in Disease
Cambridge Institute for Medical Research
Cambridge
UK

Dr. Debbie Carley
The Wellcome Trust Genome Campus
Cambridge
UK

Professor Carlos Maria Correa
University of Buenos Aires
Buenos Aires
Argentina

Mrs. Lucy Criddle
Hinxton Hall Conference Centre
The Wellcome Trust Genome Campus
Cambridge
UK

Professor Patricia Danzon
University of Pennsylvania
Wharton School of Business
Philadelphia, PA
USA

Professor Richard Feachem
Institute for Global Health
University of California Berkeley and San Francisco
San Francisco, CA
USA

Dr. Wolfram Foerster
European Patent Office
Munich
Germany

Dr. Donna Ghelfi
World Intellectual Property Organisation
Geneva
Switzerland

Ms. Malayah Harper
Department for International Development
London
UK

Dr. Christopher Hentschel
Medicines for Malaria Venture
Geneva
Switzerland

Dr. Michele Hill-Perkins
Catalyst BioMedica Limited
London
UK

Dr. Russell Howard
Maxygen, Inc.
Redwood City, CA
USA

Ms. Nina Hvid
European Federation of Pharmaceutical Industries & Associations
Brussels
Belgium

Dr. Hannah Kettler
Office of Health Economics
London
UK

Dr. Gerald Keusch
Fogarty International Center
National Institutes of Health
Bethesda, MD
USA

Dr. Richard Lane
International Programmes
The Wellcome Trust
London
UK

Ms. Tracey Lane
Performance & Innovation Unit
Cabinet Office
London
UK

Dr. Margaret Liu
Bill & Melinda Gates Foundation
Seattle, WA
USA

Dr. Richard Mahoney
International Vaccine Institute
Seoul
Korea

Dr. Malegapuru Makgoba
South African Medical Research Council
Tygerberg
South Africa

Dr. Carol Medlin
Commission on Macroeconomics
and Health
Institute for Global Health
University of California Berkeley
and San Francisco
San Francisco, CA
USA

Mrs. Olga Moreno Samper
Ciudad De La Habana
Cuba

Dr. Michael Morgan
The Wellcome Trust Genome Campus
London
UK

Ms. Lita Nelsen
Massachusetts Institute of Technology
Cambridge, MA
USA

Mr. Adrian Otten
Intellectual Property Division
World Trade Organization
Geneva
Switzerland

Dr. Ariel Pablos-Mendez
Rockefeller Foundation
New York, NY
USA

Mr

Appendix B

NOTE ON THE COOPERATION FOR DEVELOPMENT ACTIVITIES OF THE WORLD INTELLECTUAL PROPERTY ORGANIZATION (WIPO)

The World Intellectual Property Organization (WIPO) is a specialized agency of the United Nations (UN) system of organizations with responsibility to promote the protection of intellectual property (i.e., patents, trademarks, industrial designs, integrated circuits, copyright and related rights, and geographical indications) throughout the world through cooperation among member states of the UN. It is dedicated to helping to ensure that the rights of creators and owners of intellectual property are protected world wide and that inventors and authors are thus recognized and rewarded for their ingenuity.

Other than the administration of 21 treaties (two of those jointly with other international organizations), WIPO carries out a rich and varied program of work through its member states and secretariat, namely to harmonize national intellectual property legislation and procedures; to provide service for international applications for industrial property rights; to exchange intellectual property information; to provide legal and technical assistance to developing countries and other countries; and to facilitate the resolution of private intellectual property disputes and marshal information technology and the Internet as tools for storing, accessing, and using valuable intellectual property information.

One of the pillars mentioned above is WIPO's program for cooperation for development, which takes into consideration (1) the growing significance of intellectual property in support of innovation and creativity in a knowledge-intensive environment (2) the expanding implications of intellectual property, not only on economic growth but also on sustainability of social, cultural and environmental development, and (3) the progress made in many countries in connection with the establishment of the intellectual property legal framework for and compliance with the TRIPS Agreement.

The four "poles of activity" in the overall strategy for cooperation for development focus on empowering the member states to support the intellectual property system through

(a) assistance in modernization of intellectual property legislation;

(b) partnership in intellectual property administration and automation;

(c) knowledge creation; and

(d) demystification of intellectual property in the context of emerging global issues.

Item (a) focuses on strengthening national and regional capacities for upgrading intellectual property legislation in light of new developments locally and abroad. For example, WIPO's mandate to provide legal and technical assistance[16] in relation to the implementation of the TRIPS Agreement came from decisions taken by the WIPO General Assembly in its 1994 and 1995 sessions and is reflected in the Agreement of 1995 between the World Intellectual Property Organization (WIPO) and the World Trade Organization (WTO) (hereinafter referred to as the WIPO-WTO Agreement), which came into force from January 1, 1996. Furthermore, a joint initiative on technical cooperation was launched by the Directors General of WIPO and WTO in July 1998, to assist the developing countries in meeting the deadline of January 1, 2000, for implementation of the TRIPS Agreement. Both organizations reiterated their commitment to use all available resources and to provide all technical cooperation, at the request of the developing countries, to enable them to fulfill their obligations. The TRIPS deadline for developing countries has now passed and WIPO has therefore expanded its activities in the 2002–2003 biennium to supplement the WIPO-WTO Agreement.

Item (b) involves national intellectual property offices; other concerned government agencies; and right holders, users and intellectual property professionals from the research and industry sectors, especially in the provision of automation support to maximize the benefits of the intellectual property system. Together, items (a) and (b) are expected to help member states establish a complete set of institutions supporting the use and modernization of the intellectual property system. Special focus is given to the Patent Corporation Treaty (PCT), Madrid and Hague Systems, and the collective management of copyright and related rights, which will be promoted as supplementary "tools" to facilitate the acquisition of intellectual property registration and the fair distribution of its benefits by those who seek global intellectual property protection.

Item (c) concentrates on the promotion of creative and innovative activities leading to more intellectual property rights that are useful for national development, especially in the knowledge-intensive societies of today. However, the success and effectiveness of knowledge creation depend on the availability of a body of well-informed intellectual property professionals and owners and users of intellectual property, a pool of knowledgeable administrators, managers and technical staff of national intellectual property offices, and a good supply of intellectual property-related information. This brings into focus some of the important "deliverables" of WIPO's Cooperation for Development Program, notably the work of the WIPO Worldwide Academy in maintaining a pool of trained managers and staff for intellectual property administration, and the assistance of WIPO for the provision and use of the Intellectual Property Digital Library (IPDLs) and other intellectual property information and services through the WIPONET to promote inventiveness in business and industry.

Item (d) concerns the continuing drive to demystify the issues surrounding intellectual property with a view to empowering the relevant sectors of society. Basic awareness of intellectual property must reach a level in society such that creativity is sustained and encouraged and novel applications of intellectual property systems are better understood. This brings into focus the importance of undertaking developmental IP–related activities in such newly emerging areas as electronic commerce, traditional knowledge, biotechnology, biodiversity, genetic resources, and folklore, while also balancing them against activities that address current intellectual property needs and the concerns of society.

ENDNOTES

1 The main rule relating to patentability under TRIPS is that patents shall be available for any invention, whether a product or process, in all fields of technology without discrimination, where those inventions meet the standard substantive criteria for patentability — novelty, inventive step and industrial applicability (Article 27.1). In addition, signatories are required to make granting a patent dependent on adequate disclosure of the invention and may require that the patent holder provide information on the best mode for carrying it out (Article 29.1). Disclosure is a key part of the contract implied by the granting of a patent because it makes important technical information publicly available that may be useful to others in advancing technology in the area, even during the patent term. It also ensures that, after the expiry of the patent term, the invention truly falls into the public domain because others have the necessary information to make use of its information for practical application.

2 The effective period of market exclusivity is about 10 years, since it takes an average of 10 to 12 years to turn a patentable idea into a marketable product. However, in some countries, patent protection can be extended through a variety of legal means — in the US, for example, an FDA provision rewards drug firms testing the safety of their products on children with a six-month product patent extension.

3 With respect to pharmaceutical product patent protection, Watal (2001) has questioned whether in fact this observation applies to the majority of developing countries or only a few.

4 TRIPS supporters have argued that enhanced intellectual property rights protection abroad would lead to increased foreign direct investment and technology transfer to the developing world. Those opposed have rejected this view, arguing that developing countries have little to gain and in fact might be harmed if foreign competition crowds out opportunities for domestic firms to thrive.

5 The Commission on Intellectual Property Rights (CIPR) was given a one-year mandate to consider the following: how national IPR regimes should be best designed to benefit developing countries within the context of international agreements, including TRIPS; how the international framework of rules and agreements might be improved and developed, e.g., in the area of traditional knowledge and the relationship between IPR rules and regimes covering access to genetic resources; and what broader policy framework is needed to complement intellectual property regimes, including controlling anticompetitive practices through competition policy and law.

6 The others were Angola, Bangladesh, Guatemala, Kuwait, Madagascar, Morocco, Pakistan, Paraguay, Qatar, Tunisia, Turkey, United Arab Emirates, and Uruguay (Watal 2001).

7 The "pipeline" refers to the backlog of new pharmaceutical innovations awaiting market approval in a given country that may be eligible for protection if they have been patented and marketed elsewhere.

8 At the close of the WHO-WTO Workshop on Differential Pricing and Financing of Essential Drugs (April 2001), Gro Brundtland observed: "We have heard quite clearly that the price of drugs matters — it matters to poor people, and it matters to poor countries. But little progress will be possible without a significant investment in building effective health systems. We have heard too that even with lower prices — particularly in the case of anti-retrovirals — additional finance will be essential."

9 That is, provided there is no discrimination on the basis of the nationality of the persons involved, which is not the issue in the case of parallel imports.

10 Developing countries may choose from a wide range of options to respond to the affordability challenge. Many of these options are neutral with respect to intellectual property. They include participation in drug donation programs, bulk purchasing arrangements, generic production of off-patent products, and price controls. Each of these options comes with its own set of costs that must be weighed against potential benefits. None, on its own, is enough to address the current problem.

11 Tiered-pricing arrangements are permitted under TRIPS. Watal has pointed out that countries may adopt other measures, including parallel imports, price controls, and making use of the "regulatory exception" (see box, page 8). (Watal 2000). However, the use of parallel importing may undermine the implementation of differential pricing (and its political feasibility, from industry's perspective).

12 The original Ramsey solution assumed government regulation of prices because it considered a pure monopoly only. As Love has pointed out, this aspect of Ramsey pricing is not currently under consideration (Love 2001). However, Danzon (1997) refutes Love's position, arguing that Ramsey prices can be achieved in the absence of regulation if there are competing products or powerful purchasers.

13 A "march-in right" is a contractual right that allows one party to automatically be granted a license or ownership of patent rights if the other party fails to perform a specified act (e.g., fails to commercialize an invention).

14 A non-exclusive license means that others can simultaneously use and exploit the same rights under the same conditions.

15 An exclusive license means that no one other than the licensee, including the owner, can use the licensed rights and conditions.

16 From January 1996 to March 1999, the International Bureau of WIPO provided assistance, in the form of legislative advice, to a considerable number of developing countries. The assistance was rendered by the WIPO Secretariat, at the request of the countries concerned, in the form of the preparation of 136 draft laws on intellectual property subjects (20 in 1996, 54 in 1997, 42 in 1998 and 20 in the first quarter of 1999) for 78 developing countries and regional organizations. It also contributed to the preparation of studies on the compatibility of existing intellectual property laws with TRIPS obligations, preparation of draft provisions to amend and modernize existing laws in the field of intellectual property, and preparation of comments and suggestions on 130 draft laws (30 in 1996, 40 in 1997, 47 in 1998 and 13 in the first quarter of 1999) prepared by and received from 84 governments of developing countries and Secretariats of regional organizations in developing countries.

BIBLIOGRAPHY

Bale, H. E. Jr., "Patent Protection and Pharmaceutical Innovation," *Journal of International Law and Politics*, Vol. 29, No. 12, 1996/97.

Ballance, R. et al., *The World's Pharmaceutical Industries*, UNIDO/Edward Elgar Publishing, 1992.

Barton, J. H., "Rational Limits on Genomic Patents," *Nature Biotechnology*, Vol. 18, August 2000.

_____(b), "Reforming the Patent System," *Science*, Vol. 287, March 17, 2000b.

_____(c), "Patents in Genomics and Basic Research." *Issues for Developing World Health, 2001.*

Brundtland, G. H., World Health Organization Director-General, Closing Remarks at the WHO/WTO Workshop on Differential Pricing and Financing of Essential Drugs, Høsbjør, Norway, April 2001.

Correa, C., *Integrating Public Health Concerns into Patent Legislation in Developing Countries*, South Centre, Switzerland, 2000.

Danzon, P. M., "Incentivizing R&D through Differential Pricing Arrangements," working paper commissioned by Working Group 2 of the Commission on Macroeconomics and Health (CMH), forthcoming.

_____, "Price Discrimination for Pharmaceuticals: Welfare Effects in the US and the EU." *International Journal of the Economics of Business*, Vol. 4, No. 3, 1997, pp. 301-321.

_____, "The Economics of Parallel Trade," *Pharmaeconomics*, Vol. 13, No. 3, 1998, pp. 293-304.

_____, "Making Sense of Drugs," *Regulation*, Vol. 23, No. 1, 2000, pp. 56-63.

International Federation of Pharmaceutical Manufacturers Association, Internet communication at http://www.ifpma.org.

Kettler, H., *Updating the Cost of a New Chemical Entity*, Office of Health Economics, London, 1999.

Kettler, H., and R. Modi, "Building Local R&D Capacity is not Enough to Secure Investments for Neglected Diseases: The Case of India," *Bulletin of the World Health Organization*, Volume 79, 2001.

Lanjouw, J., "The Introduction of Pharmaceutical Product Patents in India: Heartless Exploitation of the Poor and Suffering." NBER Working Paper No. 6366, 1998.

Lanjouw, J. O., and I. Cockburn, "Do Patents Matter? Empirical Evidence After GATT," NBER Working Paper No. W7495, January 2000.

Lerner, J., "150 Years of Patent Protection," NBER Working Paper No. W7478, January 2000.

Lichtenberg, F. R., "The Benefits and Costs of Newer Drugs: Evidence from the 1996 Medical Expenditure Panel Survey," NBER Working Paper No. 8147, March 2001.

Love, J., "Policies That Ensure Access to Medicine and Promote Innovation, with Special Attention to Issues Concerning the Impact of Parallel Trade on the Competitive Sector, and a Trade Framework to Support Global R&D on New Health Care Inventions," comments made at the WHO/WTO Workshop on Differential Pricing and Financing of Essential Drugs, Høsbjør, Norway, April 2001.

Maskus, K., *Intellectual Property Rights and the Global Economy*. Institute for International Economics, Washington, DC, 2000.

Nelsen, L., "The Rise of Intellectual Property Protection in the American University." *Science*, Vol. 279, 1998, pp. 1460-1461.

Otten, A., Closing Remarks at the WHO/WTO Workshop on Differential Pricing and Financing of Essential Drugs, Høsbjør, Norway, April 2001.

Scherer, F. M., and J. Watal, "Post-TRIPS Options for Access to Patented Medicines in Developing Countries," working paper commissioned by Working Group 4 of the Commission on Macroeconomics and Health (CMH), January 2001.

Siebeck, W. E., ed., "Strengthening Protection of Intellectual Property in Developing Countries: A Survey of the Literature," World Bank Discussion Paper No. 112, The World Bank, Washington, DC, 1990.

Su, E., "The Winners and the Losers: The Agreement on the Trade-Related Aspects of Intellectual Property Rights and Its Effects on Developing Countries," *Journal of International Law*, Vol. 23, No. 1, 2000.

10/90 Report on Health Research. World Health Organization, Geneva, 1999.

Watal, J., "Access to Essential Medicines in Developing Countries: Does the WTO TRIPS Agreement Hinder It?" Science, Technology and Innovation Discussion Paper No. 8, Center for International Development, Harvard University, Cambridge, Mass., 2000.

_____, "Background Note for the WTO-WHO Workshop on Differential Pricing and Financing of Essential Drugs, Høsbjør, Norway, April 2001.

World Bank, *Entering the 21st Century: World Development Report 1999/2000,* Oxford University Press, New York, 2000.

Institute for Global Health
74 New Montgomery Street, Suite 508
San Francisco, CA 94105
Phone: 415/597-8200
Fax: 415/597-8299
Email: igh@psg.ucsf.edu
www.igh.org