

Patents, Biomedical Research, and Treatments:

Examining Concerns, Canvassing Solutions

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On April 12, 1955, after eight years of research and testing, Jonas Salk announced that his polio vaccine was safe, effective, and potent. The 1916 polio outbreak had left six thousand Americans dead and another twenty-seven thousand paralyzed. In the two years following vaccine release, polio cases in the United States dropped by approximately 90 percent. By 1979 no cases of polio from the wild polio virus were reported nationwide.¹ The immediate positive effect of Salk's research on the lives of thousands of Americans is uncontested. Yet despite its enormous success, the vaccine was not patented. When asked who owned the patent, Salk famously responded: "Well, the people, I would say. There is no patent. Could you patent the sun?"²

Salk's explanation for not patenting the polio vaccine would probably not convince a court of law—while he is right that no one can patent the sun, he may have been able to obtain a patent on the vaccine (neither he, his employer, nor the funder of the research ever applied for one). But it can still be assessed as an *ethical* argument—that no one *should* patent the vaccine because it should belong to everyone, just as the sun does. His argument might have been based on a belief that a patent would have had bad consequences—that it would have impeded access to the vaccine, or that, as a moral principle, certain important, lifesaving discoveries should be placed in the public domain.

Although half a century old, Salk's argument is still very much at play today. The consequences of patenting health-related discoveries for further research and for access to treatments are hotly debated, as is the morality of asserting ownership over certain kinds of discoveries—for example, those deemed lifesaving or essential for ongoing research or those deriving from the human body. The rationale generally provided for the patent system is that it encourages innovation and early stage discoveries. That is, issuing patents eventually results in the availability of knowledge and new products. But this rationale is also

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Despite its enormous success, the vaccine for polio was not patented. When asked who owned the patent, Salk famously responded: “Well, the people, I would say. There is no patent. Could you patent the sun?”

contested; some scholars, analysts, and practitioners believe that in some contexts—including sometimes in biomedicine and biomedical research—patents do little to encourage innovation and can even impede access to products and slow research.

One way of thinking about biomedical research and treatment is as an ecology in which a variety of factors and players affect whether, how, and what biomedical research is conducted and whether, how, and which treatments are delivered and to whom. Different forces play niche roles in this ecology, and patents are one such force. Yet the actual and the ideal roles of patents in this ecology are contested. Some commentators argue that patents are inappropriate, ineffective, or even harmful to innovation and access, while others argue that patents are vital to achieving these goals.

In this report we consider these debates and how they play out in the patenting of inventions involving genes and stem cells and the patenting of drugs for HIV/AIDS. We have three purposes—to educate, to analyze, and to make recommendations.

Having explained and assessed these debates, we consider laws, policies, and practices—proposed or put in place at international, national, institutional, and individual levels—that aim to preserve or create incentives for innovation in biomedicine *and* to improve inputs for further research and access to drugs. Some of these laws, policies, and practices use patents, while others employ quite dif-

ferent mechanisms. What we consider amounts not to an overhaul of the biomedical research and treatment systems, but to “tinkering” with the ecology by affecting when patents are (and are not) used to improve biomedical research and treatment, focusing in particular on stimulating innovation and improving access both to treatments and to knowledge and resources useful for further research. Recognizing that, as in all ecologies, tinkering with one part can have an effect on another, we attempt to offer both an analysis and an ethical justification for laws, policies, and practices within and outside the patent system. We conclude that any one law, policy, or practice would be unlikely to both encourage innovation and maximize access in all situations.

A commitment to both innovation and access in biomedicine and biomedical research can be onerous. It can, for instance, require that governments provide additional incentives to innovate in particular areas or that patent holders enter into creative access arrangements under which they forgo some profits or commercial opportunities because their patent happens to cover an “essential” drug or an invention that is necessary for further research. Yet access to new knowledge upon which further biomedical research can be based and to treatments for life-threatening diseases is of such fundamental importance—to individuals, nations, and the global community—that it must be one of the guiding goals for all involved.

I. Patents, Biomedical Innovation, and Access

In some senses, Salk’s story is unusual. His vaccine was developed in his university laboratory, using funds from the March of Dimes Birth Defects Foundation (then called the National Foundation for Infantile Paralysis).³ Whether driven by academic curiosity, the search for fame and glory, the desire to make a difference in the world, or a combination of all three, one thing is clear: neither Salk nor his university needed a patent as an incentive to innovate.

Once discovered, more money was needed to test the vaccine and then to manufacture and distribute it nationwide. Often, funds for this extremely expensive stage of development are invested by commercial entities on the basis of expected future profits, should the tested product reach the market. This investment may be partially se-

cured by patents, which help assure investors that no one else is developing the same product. In Salk’s case, however, the March of Dimes did not expect to recoup its investment, and so a patent was not required to bring the vaccine to market. A similar story lies behind the almost simultaneous development of another polio vaccine by Albert Bruce Sabin, which was also never patented.⁴

Yet despite the decades-long existence of an easy-to-administer, inexpensive, and unpatented vaccine, polio has persisted in many nations. In 1988, the wild poliovirus was still endemic in more than one hundred twenty-five countries on five continents, paralyzing more than one thousand children every day. It was not until early this century that polio cases were reduced to an estimated eight hundred children per year worldwide.⁵ The low cost

A History of Patents

Patents are a kind of intellectual property, which is a broad term used to refer to creations of the mind, including inventions, literary and artistic works, symbols, names, images, designs, and trade secrets.¹ Intellectual property shares many of the legal characteristics associated with real and personal property: it can be bought, sold, licensed, exchanged, or given away.

A patent is issued only when an inventor applies for one from a patent office. The application must include a description of a discovery or invention so that the patent office can assess whether the invention meets that nation's patentability criteria. If the patent is approved, the inventor receives a legal right to prevent others from making, using, or selling the invention in that jurisdiction without getting a license to do so from the inventor (in many nations the inventor is under no obligation to issue such licenses).² The right to control makes it possible for inventors to benefit from the result of their own work; otherwise, once the nature and purpose of the work was disclosed, others could easily appropriate it.³ Patents are granted for a limited time, usually twenty years from the time of filing, depending on national law. When the patent expires—when the invention goes “off-patent”—anyone may make, use, or sell the invention, within the constraints of other legal restrictions (laws and regulations covering the manufacture and sale of drugs will apply to both patented and off-patent drugs).

Modern-day patents have their origins in medieval Europe, where rulers would issue letters granting monopolies over activities, such as the production of soap or paper. The earliest known patent in England was granted by King Henry VI in 1449 to a Flemish man for a twenty-year monopoly over a method of making stained glass.⁴ In 1474, Venice became the first nation to codify its royal monopolies when it issued a statute granting ten-year monopolies for useful inventions that were new to Venice. In 1610, following allegations that royal monopolies in England were being abused, James I revoked all patents, declaring that “monopolies are things contrary to our laws.” He made an exception, however, for new inventions.⁵ The English Statute of Monopolies, passed fourteen years later, rendered illegal all monopolies except those for “new manufactures” that were not “contrary to the law nor mischievous to the State by raising prices of commodities at home or hurt of trade.”⁶

As England and other European nations expanded their empires, the patent system spread around the world. In the United States, the Constitution of 1787 explicitly authorized the granting of patents when it provided Congress with the power “[t]o promote the

Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.”⁷ Japan passed its first patent act in 1871, and Germany passed a national patent act in 1877.

Today, the U.S. Patent and Trademark Office issues three types of patent: 1) utility patents for inventions or discoveries of new and useful processes, machines, articles of manufacture, or compositions of matter, or any new and useful improvements; 2) design patents for designs for an article of manufacture; and 3) plant patents for distinct and new varieties of plant.⁸ Most of the patents relevant to this discussion are utility patents on, for example, new chemical entities, new devices, new organisms, or new processes.

To obtain a patent in the United States, or in any of the world's major intellectual property regimes, the inventor must show that the invention is useful (or has industrial applicability), nonobvious (that is, it cannot be an obvious improvement on a preexisting invention), and novel. Exact formulations of these criteria vary slightly between jurisdictions.⁹

Patents are not international. Inventors who wish to control the use of their inventions internationally need to apply for patents in many different countries, which can be time-consuming and expensive. In some cases, patents issued in one jurisdiction will not be issued in another either because that jurisdiction does not (yet) have a patent system (Swaziland lacks one, for example), because patentability criteria or the interpretation of these criteria vary from one jurisdiction to another (it was for such reasons that Canada refused to issue a patent on a mouse, already patented in the United States, that was engineered to be susceptible to cancer¹⁰), or because nations have laws preventing the patenting of some inventions (in the European system, for example, a patent application may be rejected for “moral reasons,” as described in this report).¹¹ Concerns about the impact of national variation on trade have led to treaties and guidelines seeking some level of international uniformity in patent law application. For our purposes, the most important of these is the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), which came into effect in 1995.

The overall objective of the TRIPS agreement is that: “The protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation, and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner con-

ducive to social and economic welfare, and to a balance of rights and obligations.”

Prior to the TRIPS agreement, over forty countries, including middle income countries such as Brazil and India, provided no product patent protections for pharmaceutical products.¹² This exclusion allowed some developing countries with pharmaceutical industries to manufacture exact copies of drugs covered by patents in other countries but not eligible for patents in the manufacturing country and to sell these drugs (known as “generics”) at a lower cost. Developing countries without pharmaceutical industries also benefited because they could legally import generics at competitive prices.¹³

Under the TRIPS agreement, all member countries of the World Trade Organization must, within established transition periods, ensure that their intellectual property laws provide for patents “for any inventions, whether products or process in all fields of technology.” This clause effectively closed the loophole that Brazil and India had exploited to manufacture generic drugs, and therefore threatened to make affordable generic drugs unavailable in poor nations.¹⁴ The Indian and Brazilian drug industries had made an enormous impact on international public health, with India alone producing approximately 67 percent of pharmaceutical products sold in the developing world.

Countries are also obliged under the TRIPS agreement to ensure that their laws grant patents for at least twenty years, limit the scope of exceptions to patent rights, grant compulsory licenses only under certain conditions, and effectively enforce patent rights. All developed members had one year (1996, if membership began in 1995) to amend their patent legislation, whereas developing members had five years (until 2000) and countries like Brazil and India, which did not previously recognize pharmaceutical product patents at all, had ten years (until 2005) to implement a TRIPS-compliant patent system.

The TRIPS agreement itself does not establish a uniform international patent law. While obliged to amend their laws to comply with the minimum standards in the agreement, WTO member countries also have consider-

able flexibility to develop patent and other intellectual property laws that complement their own legal systems and development needs.¹⁵ However, exercising this flexibility has proven difficult, as section III of this report makes clear.

1. World Intellectual Property Organization, *About Intellectual Property*; <http://www.wipo.org/about-ip/en/> (accessed June 7, 2006).

2. T.G. Field, Jr., “What is Intellectual Property?” January 2006; <http://usinfo.state.gov/products/pubs/intelprp/> (accessed June 7, 2006).

3. Commission on Intellectual Property Rights, “Integrating Intellectual Property Rights and Development Policy,” 2002 http://www.iprcommission.org/graphic/documents/final_report.htm (accessed June 7, 2006).

4. The U.K. Patent Office, “Origins,” *Patents*, <http://www.patent.gov.uk/patent/whatis/fivehundred/origins.htm> (accessed June 7, 2006).

5. *Ibid.*

6. Statute of Monopolies 1624 (England), Section 6.

7. Constitution of the United States, Article 1, Section 8.

8. 35 United States Code 101.

9. L.B. Andrews, “Genes and Patent Policy: Rethinking Intellectual Property Rights,” *Nature Reviews Genetics* 3, no. 10 (2002): 803-808.

10. *Harvard College v. Canada (Commissioner of Patents)* [2002] 4 S.C.R. 45, 2002 SCC 76.

11. E.R. Gold, “Biotechnology Patents: Strategies for Meeting Economic and Ethical Concerns,” *Nature Genetics* 30 (2002): 359.

12. Haochen Sun, “The Road to Doha and Beyond: Some Reflections on the TRIPS Agreement and Public Health,” *European Journal of International Law* 15, no. 1 (2004): 123-50.

13. S. Kontic, “An Analysis of the Generic Pharmaceutical Industries in Brazil and China in the Context of TRIPS and HIV/AIDS,” http://www.law.utoronto.ca/documents/ihrp/HIV_kontic.doc.

14. J. Barton, “TRIPS and the Global Pharmaceutical Market,” *Health Affairs* 23, no. 3 (2004): 146-54.

15. C. Correa, “Integrating Public Health Concerns into Patent Legislation in Developing Countries,” (Geneva, Switzerland: The South Center, 2000); J.H. Reichman, “Taking the Medicine with Angst: An Economist’s View of the TRIPS Agreement,” *Journal of International Economic Law* 4, no. 4 (2001): 795-807.

of the unpatented vaccine was clearly not enough to ensure universal access to it.

The story of the polio vaccine is not the story of all new drugs and treatments, many of which use patents to secure commercial investment to bring them “from bench to bedside.” But it is not an entirely unique or outdated model, either. There is no one model for the funding and conduct of biomedical research or the development and provision of medicines and treatments, and there is no one model for the role of patents in these processes. Patents provide an incentive for some biomedical research, but sometimes they play a much more limited

role. Similarly, they are important for securing the funds to turn some early discoveries into products and to distribute them to those in need, but they are not always necessary, and although they can ensure that knowledge is disclosed to the public, they can also prevent individuals and institutions from using that knowledge. Discerning when patents are important, how they should be managed, and when they are unnecessary or even damaging is difficult and debated. Getting clear on the uses and limits of patent systems is, however, crucial for the development of effective and ethically defensible law, policy, and practice.

The Bigger Picture: Health, Biomedical Research, and Treatments

Despite great progress in identifying, treating, curing, and preventing disease and disability, millions worldwide still suffer ill health. Safe and effective treatments do not exist for many conditions, and according to the World Health Organization, one-third of the world's population lacks access to existing essential drugs—a figure that surpasses 50 percent in some parts of Asia and Africa.⁶ This treatment access problem has at least three explanations in any particular case: (1) individuals or nations cannot afford existing treatments; (2) nations lack the infrastructure or political will to acquire and distribute the treatments that they can afford; (3) the appropriate treatments do not exist. As we will see, patents may or may not contribute to these problems.

(1) Individuals or nations cannot afford existing treatments. The gap in wealth between rich and poor countries can be illustrated most dramatically by examining disparities in global health indicators. Maternal mortality in the world's least-developed countries is fifteen times the rate of that in industrialized countries. Average life expectancy in the developed world is seventy years, in many developing countries less than fifty years,⁷ and in some African countries, particularly those ravaged by HIV/AIDS, less than forty years. Three diseases—HIV/AIDS, tuberculosis, and malaria—together kill approximately six million people per year in developing countries, accounting for more than a third of the annual death toll in these regions. In 2004, average per capita health expenditures in the developing world as a whole were the equivalent of \$98, compared to an average of more than \$3,800 in industrialized countries. An estimated 1.5 billion people are not expected to survive to the age of sixty, and more than 880 million people lack access to health services.⁸

Cost is one of the many reasons individuals around the world—in both developed and developing countries—lack access to treatments. The price of a treatment, particularly a drug, is influenced by many factors, including where, when, and how it was discovered, developed, manufactured, and distributed, as well as whether and where it is patented. Some treatments cost a lot to discover and develop, and they may be priced to recover that cost. Some drugs, regardless of their initial discovery and development costs, are simply more expensive to make and distribute than others. The price of a treatment in a particular country is also affected by how much people are willing and able to pay for it.

The presence of a patent (or patents) on a treatment or on the products or processes involved in that treatment can also affect its price. If a product or process is patented in a jurisdiction, the patent holder or any licensees can control who sells that treatment in the jurisdiction. Fewer

licensees means greater power to price the treatment without reference to competitors (although in some markets, price controls or negotiations with large purchasers, including governments, may constrain prices). Drugs, vaccines, and other treatments that are covered by patents are almost always more expensive than their off-patent counterparts.

Yet even in the absence of patents, treatments are seldom free. Drugs and devices must be manufactured (some are expensive to make) and distributed and sometimes require specialist knowledge to be administered, all of which contributes to their price. And usually, at least some profit must be possible if manufacturers and distributors are to enter the market at all. In rare instances, all these costs are covered by a national government or a national or international aid organization (such as WHO or The Bill and Melinda Gates Foundation), and treatments are then greatly subsidized, even free. At other times, even when treatments are sold at or only slightly above manufacturing cost, they may still be too expensive for millions of the poorest individuals and countries worldwide.

(2) Nations lack the infrastructure to adequately distribute the treatments that they can afford. Unfortunately, access problems may persist despite the availability of appropriate treatments that are inexpensive or free. For example, a recent study examining fifty-three African countries found that patents were not the primary reason that people lacked access to antiretroviral drugs.⁹ The study's authors, Amir Attaran and Lee Gillespie-White, argued that poverty, the high cost of the drugs, national regulatory requirements for medicines, tariffs and sales taxes, and above all a lack of sufficient international financial aid to fund the treatment posed greater barriers to access than patents *per se*.¹⁰ The study's methodology was criticized, but it nonetheless made an incontrovertible point: patients in poor countries often do not receive adequate access even to those drugs that are no longer patented.¹¹ In fact, the majority of products on WHO's list of essential medicines—which includes many drugs used to treat various aspects and side effects of HIV/AIDS—are now off patent, yet they remain unavailable or unaffordable to most of those suffering from the virus.¹²

Differences in health status between poor and rich countries are caused not just by the diseases that are prominent, but also by the quality of the health system.¹³ Health systems must, in addition to providing basic treatments, attend to public health, vaccinations, sanitation, water safety and quality, nutrition, and reproductive health. They must also operate efficiently, effectively, and fairly. Otherwise, the safe delivery and administration of treatments (even if provided freely) will be difficult or impossible. As one commentator recently observed, "Even if we had free and unlimited supplies of ARVs and other essential HIV/AIDS commodities, they still would not be

Health infrastructure problems are not the fault of the patent system, but going some way toward addressing them is necessary to make even cheap or free treatments reliably available to those who need them.

available to the majority of people who need them because of poor infrastructure.”¹⁴

Health systems must also seek to ensure that available treatments meet quality standards. Surveys from several developing countries show that 10 to 20 percent of sampled drugs fail quality control tests.¹⁵ Fewer than one in three developing countries are estimated to have fully functioning drug regulatory authorities, which is part of the reason that growing numbers of fake drugs are entering these countries. Between 25 and 50 percent of medicines sold in the developing world are estimated by WHO to be counterfeit.¹⁶ Further, a World Bank study found that “inefficiencies in the procurement, storage, prescribing, and use of drugs are so extensive . . . that consumers in some countries get the benefits of only \$12 worth of drugs for each \$100 spent on drugs by the public.”¹⁷

Unfortunately, political will is often in short supply.¹⁸ For example, despite the huge numbers of deaths from preventable diseases in African countries each year, African governments spend an average of only 3 percent of their gross national product on health care (while the United States spends approximately 14 percent).¹⁹ These countries spend more on their military than on health care.²⁰

None of these infrastructure problems are the fault of the patent system, and going some way toward addressing them is necessary to make even cheap or free treatments reliably available to those who need them.

(3) The appropriate treatments do not exist. Of course, the access problem may not just be affordability; people all over the world suffer and die from conditions for which efficacious treatments do not even exist. In particular, there is an acknowledged lack of new treatments and vaccines for diseases that primarily affect people living in poor countries. An estimated 90 percent of the \$56 billion spent annually on health research by the public and private sectors goes toward diseases that afflict just 10 per-

cent of the world’s population.²¹ In the last twenty-five years, almost fourteen hundred new medicines were developed, but only 1 percent of them were for tropical diseases that kill millions each year.²² The research and development pipelines for new drugs for diseases like tuberculosis, African sleeping sickness, and leishmaniasis are virtually empty. Where drugs exist to treat these illnesses, they are often old, ineffective (including against new, drug-resistant strains), and sometimes difficult to administer in resource-constrained environments. Some vaccines require refrigerated storage, for example, yet there are no such facilities in many rural parts of the developing world.

Sometimes the absence of effective treatments is not for lack of trying, but for many conditions—particularly those that affect very few people or mainly poor people—the absence is likely explained by market forces. The bottom line is that poor countries are seldom profitable markets; they are simply unable to pay for, or properly distribute and monitor, many treatments. Developing drugs and other treatments for conditions that are prevalent primarily in these countries can be a financial loser. The same is sometimes true for treatments for unusual diseases and conditions, for which the market, even in the developed world, can be too small to attract investors.²³ Again, the patent system is not to blame. Providing additional incentives (other than potential patents and profits from sales) for biomedical research that targets neglected diseases, or that seeks better ways to deliver existing treatments, may be the only way to stimulate innovation in these areas.²⁴

In sum, to significantly improve the health status of their citizens, countries need strong and well-run health systems and disease prevention programs; well-functioning drug approval, procurement, and distribution programs; sufficient numbers of well-trained health personnel; and the political will to address health problems. They also need affordable access to new and existing treatments.

II. The Biomedical Research Context: Genes and Stem Cells

Biomedical research and the development of treatments both involve many stages, any of which can yield patentable inventions and discoveries. Some of these inventions and discoveries are useful in further research, such as newly identified genes that generate a particular protein; while others will likely be used in treatments following additional development, such as new chemical entities that could eventually be marketed as drugs. Some inventions are useful both as they stand and following further development; for example, genetic markers for breast and ovarian cancer can be useful in ongoing research and for screening potential sufferers.

The biomedical research generating these inventions is funded in a variety of ways and conducted by a variety of individuals and institutions. Some research is funded by companies, other research by governments, international charitable organizations, private foundations, and other organizations. Funders may be motivated by a desire for specific products, such as a malaria vaccine or a new treatment for diabetes, or by the quest for greater knowledge in basic biomedical science, such as of cell differentiation or gene-environment interaction. Of the biomedical research funded by nonprofit entities, a significant portion is funded by national governments and is conducted in academic institutions. In 2002, the United States federal government provided \$19 billion to academic institutions for research and development, of which two-thirds came from the U.S. National Institutes of Health.²⁵

The importance that parties attach to obtaining patents on inventions and discoveries also varies. Where the research is funded or conducted by a company, the company may seek patents to recoup the costs of their initial research and eventually to generate a profit. Where the research is funded by a government or charitable organization or conducted in a nonprofit institution, such as a university or an independent research institute, recovering the original research costs may not be necessary and a profit may not be expected. Nevertheless, in the United States and increasingly in other countries, laws and policies encourage the recipients of government and other funding to patent the results of their research on the grounds that patented inventions are more likely to be picked up by industry and further developed into new products.²⁶

Some inventions and discoveries resulting from biomedical research have always been patented—by both for-profit and not-for-profit researchers (many of whom are legally obliged to immediately assign their patents to their employers). But in the past twenty-five years, the number of biomedical patents has dramatically increased worldwide, including on biological materials and on inventions or discoveries that are still at early stages of development.

The Increase in Biomedical Patenting

From 1990 to 2003, the number of U.S. patents granted annually increased over 100 percent, from about 80,000 to 169,000 per year.²⁷ During a comparable period, patent applications to the European Patent Office and the Japanese Patent Office also increased significantly.²⁸ While this increase has covered many areas, it has been particularly significant in the biological sciences, and within that field, in genetics. A 2002 survey commissioned by the National Science Foundation reported that the total number of “international patent families” on human DNA sequences (defined as groups of patents associated with a single invention) tripled from the early to late 1980s and nearly tripled again during the early and late 1990s. Although the increase occurred worldwide, the survey found that “[t]hroughout this 20-year period, the United States led all other nations and the 15-nation European Union (EU) with 72 percent of total international patent families formed.”²⁹

A recent survey by Kyle Jensen and Fiona Murray focusing on the United States reports that 20 percent of the over twenty-three thousand known human genes listed in the National Center for Biotechnology Information’s database are the subject of 4,270 U.S. patents (in over three thousand patent families).³⁰ These patents are owned by over eleven hundred different institutions, individuals, or companies, based both in and outside the United States. Although these numbers indicate that a large portion of the human genome is unpatented, some important genes are heavily patented, including genes associated with increases in breast cancer, diabetes, and obesity³¹—three diseases that exert a heavy toll in the developed world (and therefore represent potentially profitable markets for new treatments).

These increases in “gene patenting” have many causes, including increased investment in genetics by the international biotechnology industry and by governments, yielding correspondingly more inventions and discoveries. Some of the government-funded research has been under the recently completed international Human Genome Project and on an ongoing basis from the U.S. National Human Genome Research Institute at the National Institutes of Health and from the U.K.’s Wellcome Trust. Advances in technology and an increased propensity among those conducting the research to file for patents on this kind of invention and discovery have also contributed to the increase.

Around the world, new laws and changes in academic culture and practice have led to more patenting in all kinds of research, including biomedical research.³² Perhaps because it was the first nation to alter its domestic law on the issue, the United States leads the world in academic patenting.³³ The United States’ 1980 Bayh-Dole

The overall number of biomedical patents issued worldwide is on the rise. This increase, and the emergence of patents in areas like genetics and stem cell research, has led to calls for changes in the laws, policies, and practices that bear on patent systems.

Act states that institutions receiving federal funds may elect to retain title to any inventions resulting from a federal grant, contract, or cooperative agreement, subject to certain restrictions, including that the government retains a nonexclusive license to any inventions and that institutions share royalties with individual inventors (usually university faculty).³⁴ That same year, the U.S. Congress gave government agencies the power to patent the results of their in-house research.³⁵ In the ten years since 1995, the NIH alone has been awarded an average of one hundred twenty-two U.S. patents per year.³⁶ Patents awarded to U.S. academic institutions quadrupled between 1988 and 2003, rising from approximately eight hundred to more than thirty-two hundred patents issued per year (for biomedical and other inventions).³⁷

These “academic” patents are said to be necessary, not to recover the costs of the initial research, but to encourage industry—often through exclusive licensing of the patented invention—to pick up the results of the research and translate them into new products.³⁸ Without a patent and the ensuing exclusive license, some have argued, companies, particularly pharmaceutical companies, will not be interested in investing the resources to develop inventions or discoveries generated with public or other monies. These patents also allow the institution and the individual inventor to generate additional income. But some critics argue that patenting and licensing by nonprofit institutions have had a negative impact on access, both to end products such as drugs and diagnostic tests and to information and materials useful in further research, such as genes or methods of deriving stem cells. Thus patenting and licensing fees have sometimes hindered innovation.³⁹

As more biomedical patent applications have been filed, more of these applications have been granted, in part due to the evolution of patent law. Most nations have strengthened their patent regimes over the past decade, sometimes in order to comply with the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), but also in hopes that stronger patent laws encourage innovation.⁴⁰ Changes in the world’s three major patent systems—those of the United States, Europe, and Japan—have expanded the coverage of patent protection, led to broad patents in new areas, restricted the use of research exemptions, and encouraged courts to enforce the rights of patent holders.⁴¹

The U.S. patent system is known for its openness to granting patents. There are a number of reasons for this flexibility, including case law and policy and practice at the U.S. Patent and Trademark Office (USPTO). In the United States, patents have been issued on naturally occurring substances since the 1912 decision that adrenalin could be patented provided it was isolated from its natural source.⁴² In 1980, the U.S. Supreme Court in *Diamond v. Chakrabarty* expanded patentability criteria to include some living organisms. The case involved a claimed patent on a genetically engineered bacterium that was capable of breaking down crude oil. In a five to four ruling, the Court held that patents could be awarded on living organisms provided that the organisms had been sufficiently manipulated by the inventor:

The patentee has produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature’s handiwork, but his own; accordingly, it is patentable subject matter.⁴³

Since then, higher life forms have also been the subject of patent applications. In 1988 and 1992, Harvard University obtained patents in the United States and European Union respectively on the “oncomouse”—a mouse genetically engineered to be susceptible to cancer. Not all jurisdictions have accepted this patent, however; the Supreme Court of Canada denied it on the ground that the mouse was a higher life form and not a “composition of matter,” as required under Canada’s Patent Act.⁴⁴

While not all jurisdictions will issue the same patents, the overall number of biomedical patents issued worldwide is on the rise. This increase, and the emergence of patents in areas like genetics and stem cell research, has led to calls for changes in the laws, policies, and practices that bear on patent systems.

Current Concerns: Patentability, Morality, and Access

The increase in biomedical patents has fueled a number of concerns, which broadly fall into two categories: concerns about the legality and morality of patenting certain kinds of inventions, and concerns about the consequences for the biomedical research and therapeutic contexts.

Where patents have claimed isolated biological substances, including genes or cell lines, critics have claimed that these naturally occurring substances, even when isolated, do not meet the legal requirements of novelty or, in some cases, nonobviousness. In the case of patents on isolated genes, for instance, it has been argued that the useful properties of the substance are not invented by the scientist but are “natural, inherent qualities of genes themselves.”⁴⁵ This argument has also been applied to cell lines. In addition, now that DNA sequencing has become relatively quick and easy to do, some have argued that isolating a portion of DNA no longer meets the patentability criteria of nonobviousness because isolating the gene would have been obvious to a skilled person working in the field.⁴⁶ When it comes to interpreting the patentability criteria, the U.S. courts and USPTO have taken a particularly expansive view.

Questions have also been raised about the application of patent law. An analysis by Jordan Paradise, Lori Andrews, and Timothy Holbrook of seventy-four U.S. patents containing over one thousand claims related to human genes determined that 38 percent of the claims did not meet the legal criteria for patentability. According to the authors’ interpretation of the law, the most frequent problem was that the patents “claimed far more than the inventor actually discovered.” Other problems included claims of unproven utility, or claims of a correlation between two things, such as a mutation in a gene and a disorder, without showing that the mutation caused the disorder.

Some errors are to be expected in the granting of patent applications, but based on their results, Paradise, Andrews, and Holbrook suggested that the USPTO institute specialist training for patent examiners in DNA-based technologies, introduce additional safeguards to ensure that patent applications are sufficiently examined, and possibly alter its financial incentives. “Currently, patent examiners are encouraged with monetary bonuses to grant patent applications, a policy that has the unsettling effect of rewarding examiners for quickly pushing patents through the patent office.”⁴⁷ Although other jurisdictions organize their patent offices differently, similar problems may nonetheless plague gene patents and other biomedical patents issued outside the United States. The Paradise study’s concerns and recommended responses suggest that all patent regimes should consider specialist training for examiners working in genetics and other novel, specialized areas, and that periodic review of the application of patentability criteria is necessary to ensure that they are being correctly applied.

Critics have also argued that, regardless of the legal patentability criteria, certain inventions *should not* be patented. Where patents involve human biological substances, some have asserted that these substances should not be patentable under law (or that, regardless of the law, inventors should not apply for patents on them) because

they already belong to “humanity”—they are “our common heritage”—and patenting them inappropriately commodifies the human body.⁴⁸ A counter to such arguments is that they rely on moral positions not necessarily shared by most members of society (a claim that ought to be open to empirical analysis within jurisdictions).

One way to recognize this argument is to legally exclude from patentability those inventions that threaten “*ordre public*” or common morality. The TRIPS agreement permits this move. Although U.S. law does not currently accommodate objections based on such concerns,⁴⁹ the European Patent Convention contains this exclusion⁵⁰ and the European Biotechnology Directive on the legal protection of biotechnological inventions prohibits patents on processes for cloning humans, the modification of the human germ line, and the use of embryos for industrial or commercial purposes (a provision that has prevented patents on human embryonic stem cells).⁵¹

Not surprisingly, interpreting this morality exclusion could be difficult. In its report on the ethics of patenting DNA, the U.K.’s Nuffield Council on Bioethics noted that evaluating patent applications by weighing their impact on “*ordre public*” and “morality” will require expertise that is generally not represented in patent offices.⁵² Despite these difficulties, this kind of objection has been successfully raised in Europe, which suggests that the expertise to address it in particular cases can be developed. Certainly, if feelings about the morality of patenting certain kinds of invention run high, a morality-based legal exclusion will be the most effective way to prevent such patenting. Whether the exemption is desirable will very much depend on what is valued in a given jurisdiction: the exemption might slow a line of innovation by removing the incentive of obtaining a patent, but this result could be considered an acceptable price to pay in a society committed to keeping human bodily materials out of the commercial realm. Even where the law does not provide this exclusion, morality-based objections might nevertheless persuade some inventors not to seek patent protection or, if a patent is issued, to make the invention widely available. Morality arguments may affect practice even if they cannot alter the law.

Access for Further Research and Innovation

These concerns—that patents involving genes and other biomedical inventions might improperly stretch (and sometimes might not meet) the legal criteria for patentability, and that such patents are immoral—have been joined by concerns about the consequences of these patents for further research and treatment. Specifically, the concern is that because patent-holders have the power to prevent others from making or using their inventions, they effectively have the power to inhibit or prevent research and therefore slow or prevent innovation.

In theory, patenting and licensing biomedical inventions that might be useful in further research could facilitate innovation. The possibility of obtaining a patent encourages investment in research in new areas, and once issued, the patent provides the basis for seeking the investment for further research and development. Patents involving isolated genes and methods of deriving cell lines, for example, are the “products” of numerous biotechnology companies, which license these inventions to generate the funds to conduct further research.

But patenting and licensing could also impede further research if it creates a “tollbooth” through which researchers must pass.⁵³ Some inventions, such as those involving genes or broadly described methods of deriving embryonic stem cells, are essential for further research. But if these licenses are expensive, the research may be too costly to pursue, and if a great many licenses are required, negotiating all the licenses might be prohibitively difficult and time consuming as well as expensive.

Some critics assert that human biological substances should not be patentable because they already belong to “humanity”—they are “our common heritage”—and patenting them inappropriately commodifies the human body.

But how valid are these concerns? The U.S. debate about them is not finished. During the 1990s, there were reports that academic researchers were having trouble gaining access to materials or were being prevented from using processes generated by other laboratories.⁵⁴ These access problems were thought to have arisen when patent holders refused to share their patented materials and processes or required costly and time consuming negotiation of licenses necessary for research to go forward. In 1998, Michael Heller and Rebecca Eisenberg described this access problem as “the tragedy of the anticommons,” whereby “[a] proliferation of intellectual property rights upstream may be stifling life-saving innovations further downstream in the course of research and product development.”⁵⁵ As Heller and Eisenberg described it, when a researcher needs access to multiple patented inputs to create a single useful product, “[e]ach upstream patent allows its owner to set up another tollbooth on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation.” This concern was also echoed in 2002 by the U.K.’s Commission on Intellectual Property Rights.⁵⁶

In the late 1990s, the U.S. National Institutes of Health was so concerned about the possibility that patents were stalling research that it established a working group to focus on what it called “research tools,” defined as “the full range of resources that scientists use in the laborato-

ry.” In its 1998 report, the group noted that “[a]lthough competitive pressures have always given scientists an incentive to withhold new research tools from their rivals, past practices allowed for relatively free exchange, typically without formal agreements and without explicit consideration of commercial rights or potential financial benefits.” It concluded that “many scientists and institutions involved in biomedical research are frustrated by growing difficulties and delays in negotiating the terms of access to research tools,” and it urged the NIH to promote free dissemination whenever possible.⁵⁷

In response, the NIH issued guidelines stating that recipients of NIH funds are expected to ensure that unique research resources are made available to the scientific research community. In particular, the guidelines stated that research tools need not always be patented, and that if they are patented, they should seldom be licensed exclusively to one individual or organization. When an exclusive license is considered necessary to ensure further de-

velopment, the guidelines recommended that it be limited to a particular commercial field, allowing the patent holder to use and distribute the tool for other research.⁵⁸ The NIH followed these guidelines in 2004 with its “Best Practices for the Licensing of Genomic Inventions,” in which it makes similar recommendations to its funding recipients about patenting and licensing of a wide array of genetic materials and technologies, including sections of DNA, methods for the sequencing of genomes, and the detection of genetic mutations and genetic modifications.⁵⁹

The NIH’s guidelines and best practices are not laws and are directed only at institutions receiving NIH funds, the vast majority of which are universities, colleges, and nonprofit research institutions. Nevertheless, if adopted by these institutions—and particularly if applied to all research findings rather than only to research tools and genomic inventions generated using government funds—they could have a major impact on access.

In 2006, the Organisation for Economic Co-Operation and Development, in guidelines it issued for the licensing of genetic inventions, made recommendations very similar to those of two NIH guideline documents. The OECD guidelines attempt to shape the practice of all patent holders, however, not only of those whose inventions were generated using public monies.⁶⁰ The rationale for restricting guidelines to genetic inventions (although

The Example of Stem Cells

Against the background of a decade of controversy over patents involving human genes came the 1998 derivation of pluripotent stem cell lines from human embryos by James A. Thomson and colleagues.¹ Their research generated both great scientific interest and, because it involved the destruction of early human embryos, much public controversy. In the United States, it also led to two important patents on a purified preparation of primate embryonic stem cells, a purified preparation of human embryonic stem cells, and a method for isolating each.² The patents were issued to Thomson as inventor and assigned immediately by him to the Wisconsin Alumni Research Foundation, which handles intellectual property generated at Thomson's workplace, the University of Wisconsin-Madison.

Concerns about the morality of the patents. The criticism of these patents—and subsequent patents involving human embryonic stem cells—is much like that directed at patents involving human genes. Three claims are paramount: that the declared inventions do not all meet the patentability criteria, that the patents will impede access for research and future treatment, and that patents should not be issued on this subject matter for moral reasons. Because they include rights to cells taken from human embryos that are destroyed in the process of removing the cells, one U.S. senator views such patents as “akin to slavery”³ (although the patents do not actually cover human embryos themselves). The necessary connection between some of the inventions claimed in these patents and human embryos has resulted in similar patents being challenged or not issued at all in other jurisdictions.

When the European Patent Office granted a patent to the University of Edinburgh in 1999 on a method of using genetic engineering to isolate animal stem cells, a protest erupted and a challenge to the patent was lodged.⁴ The challenge was successful on several grounds, including that it was contrary to the European Patent Convention, which excludes from patentability uses of human embryos for industrial or commercial purposes and inventions contrary to “ordre public.”⁵ The University of Edinburgh initially amended its patent application to exclude human embryonic stem cells, but it later reversed its position and launched an appeal, which has not yet been decided. In the meantime, at least two other patent applications involving human embryonic stem cells have been rejected by the European Patent Office on the basis of its Edinburgh decisions.⁶

Concerns about access and control. Embryonic stem cell patents also raise concerns about access to the materials and processes needed for further research and treat-

ment. In the United States, the Thomson patents have been described as effectively covering “all [embryonic stem] cells and downstream products, regardless of how the cells are derived.”⁷ Broad patents are not unusual in new areas of science and technology, and they are arguably an appropriate reward (and incentive) for entering into uncharted territory. Nevertheless, the Thomson patents have been criticized for their breadth and for the power they give the patent holder, who effectively controls all subsequent human embryonic stem cell research and any treatments that might result before the patent expires.

The extent of this power became evident in 2001 when the U.S. National Institutes of Health began to set up a registry listing all embryonic stem cell lines that meet President Bush's federal funding policy. To facilitate the use of these lines, the NIH negotiated with The Wi-Cell Research Institute (to which the Wisconsin Alumni Research Foundation had assigned the patent rights) to ensure that researchers who signed a standardized agreement could use the registry's lines without breaching the Thomson patent. Under the agreements, Wi-Cell makes the patented lines and derivation method available to noncommercial, federally funded researchers royalty free (Wi-Cell seeks a nominal charge when asked to supply actual materials). But if researchers wish to commercialize their work, they must negotiate new licenses, as must all researchers—commercial and noncommercial—who wish to study embryonic stem cells using nonfederal funds. Without these licenses, researchers risk a patent infringement suit, although such a suit might not be completely successful if, as some legal scholars believe, aspects of the Thomson patents are open to challenge⁸ (in fact, these patents are being legally challenged as we go to press).

The Thomson patents highlight the control that patent holders (who may or may not be the inventor) can have over a field of research by means of licensing practices. At first, WARF seemed to be fairly accommodating: although it retained a tight hold on future commercial rights, it issued nonexclusive licenses to many researchers. But recently some researchers have complained that access is not as easy and cheap as they wish it were.⁹ Critics also accused WARF of being unreasonable and aggressive when it asserted that if a U.S. state benefited from its role in funding stem cell research, as California proposed to do, then it would consider that research commercial and would require a more expensive commercial license. As stem cell research progresses and the distinction between commercial and noncommercial use blurs, the exercise of patents rights are, per-

haps predictably, becoming an issue in the stem cell debate.

Attempts to force benefit sharing. Another twist on patent issues in stem cell research occurred in 2004. When California voters agreed to use \$3 billion worth of state bonds to fund stem cell research, they also agreed that “[a]ll grants and loan awards be subject to intellectual property agreements that balance the opportunity of the State of California to benefit from the patents, royalties, and licenses that result from basic research, therapy development, and clinical trials with the need to assure that essential medical research is not unreasonably hindered by the intellectual property agreements.”¹⁰ Implementing this restriction is proving challenging, and critics have charged that restrictions might discourage innovation and investment, and that the additional benefit sharing is unnecessary anyway because the state’s citizens will benefit sufficiently from new and better treatments.¹¹ While the restriction asserts that the funders of the research that led to the patent (the State of California) should benefit from whatever income the patent produces, it does not specify how that benefit-sharing should occur.

Currently, the body entrusted with distributing the state’s stem cell funding has proposed translating the original benefit sharing language into a policy whereby all nonprofit organizations would own any intellectual property arising from their research, but recognizing that this intellectual property would be “shared broadly and promptly with the scientific community,” would be licensed nonexclusively where possible, would be subject to the march-in rights if underutilized, and would “be made freely available for research purposes in California research institutions” (an effective exemption from patent infringement for academic research use within a specific geographic territory).¹² This proposal, which would function as a condition of receiving state funding, does not include a requirement to share royalties, but it does include many elements of the practice recommendations made by the NIH and the Organisation for Economic Cooperation and Development for genetic inventions and research tools. It has been criticized for not seeking to limit the costs of any stem cell treatments resulting from the state-funded research. The overall issue is still not resolved.¹³

Plainly, stem cell research shows how patents generate concerns both about morality and about whether patents may limit access to the materials and processes needed for further research and treatment. To date, the former concerns have led some jurisdictions to refuse patent ap-

plications involving embryonic stem cells, which some analysts feel has had a chilling effect on research in those jurisdictions (although it is difficult to tell which jurisdiction-specific factors are responsible for research investment). Access for further research and treatment has thus far not been a significant problem, in large part because of the practices of the patent holders or the absence of patents, depending on the jurisdiction in question. However, if embryonic stem cell research leads to a profitable treatment before the broad Thomson patents expire or are overturned, and if the Thomson patent holders seek royalties that drive up the cost of such treatments, attention may return to the patents themselves and the expectations and practices of those who control them.

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2. U.S. Patents 5,843,780 and 6,200,806.
3. A. Pollack, “Debate on Human Cloning Turns to Patents,” *New York Times*, May 17, 2002.
4. M. Rimmer, “The Attack of the Clones: Patent Law and Stem Cell Research,” *Journal of Law and Medicine* 10, no. 4 (2003): 448-505.
5. Convention on the Grant of European Patents (European Patent Convention), Article 53(a).
6. P.M. Webber, “Patentability of Human Embryonic Cells under the EPC,” http://pharmalicensing.com/features/display/1119630334_42bc33fe14906 (accessed September 14, 2005).
7. S. Rabin, “The Gatekeepers of hES Cell Products,” *Nature Biotechnology* 23, no. 7 (2005): 817-19, at 818.
8. *Ibid.*
9. J.M. Simpson, “WARF Should Stop Impeding Research,” *Wisconsin State Journal*, June 26, 2006. G. Blumenstyk, “A Tight Grip on Tech Transfer,” *Chronicle of Higher Education*, September 15, 2006.
10. State of California. “Proposition 71: Text of Proposed Law,” http://www.ss.ca.gov/elections/bp_nov04/prop_71_text_of_proposed_law.pdf.
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12. California Institute of Regenerative Medicine, “Notice of Proposed Regulation Adoption, California Code of Regulations, Title 17.—Public Health, Division 4—California Institute For Regenerative Medicine,” chapter 3, May 5, 2006, http://www.cirm.ca.gov/laws/pdf/ip_oal_nonprofit.pdf.
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this term is given a wide definition in the document) is not clear, and it may well be that many of the OECD’s recommended practices could, and in some cases should,

be applied to all biomedical inventions (this point is discussed further in section V below).

Given the widespread patenting of biomedical inventions and the concern about the effects of those patents,

one might expect that many biomedical researchers are today prevented from pursuing research due to patents controlled by other researchers, academic institutions, or companies. Yet there is less evidence of patents slowing down biomedical research than one might imagine. In 2005, John P. Walsh and colleagues published a survey of over four hundred biomedical researchers in U.S. universities, government, and nonprofit research institutions. They sought information on researchers' patenting activities and experiences obtaining permission from others to use materials and processes in their research. The survey revealed that of those researchers who knew that their research involved another's patent, none reported abandoning a line of research. In addition, very few reported making modifications to research design or sustaining delays due to another's patents, and of those who sought a license for use of another's technology, all but one reported obtaining permission to use the technology for free. Walsh et al. concluded that, "for the time being, access to patents on knowledge inputs rarely imposes a significant burden on academic biomedical research."⁶¹

However, the Walsh study also reported that when it came to using another's research materials—substances that must be physically shared, such as cell lines or model organisms, not just intellectual property—access was sometimes delayed or denied altogether. "Over a 1-year period, an average of one in six respondents reported that delays in receiving materials from other academics caused at least one project they were working on to suffer a greater than 1-month delay, a substantial delay in a fast-moving research field. Noncompliance by other academics with research input requests resulted in about 1 in 14 scientists abandoning at least one of their projects each year." Reasons given for refusals or delays were that compliance was costly and time consuming for the holder of the materials, but Walsh et al. also established a correlation between refusals to supply materials and the presence of commercial interests in those materials (although not specifically patents).⁶²

Other reports have had other results, however. A survey conducted by the American Association for the Advancement of Science of its own members found that 40 percent of respondents reported difficulties in obtaining access to patented technologies, and over half of these said their work was delayed or needed to be changed.⁶³ And although the Walsh findings somewhat assuage the concern that patents are hindering research, the study also found that only 5 percent of researchers regularly checked whether there was a patent on the material or process they were employing in their research, and only 5 percent reported that they or their institution had received a notification letter citing patent infringement.⁶⁴

These findings about proceeding without checking for patents and without obtaining licenses may evidence a broad commitment to the norm of communalism and the practice of sharing knowledge.⁶⁵ They also suggest that U.S. academic biomedical researchers and patent holders frequently behave as though there were an exemption in patent law for academic research, even though a recent U.S. court decision clarified that such an exemption does not exist.⁶⁶ A research exemption does exist under statute in some countries, including Japan, Korea, Mexico, Turkey, and many EU countries.⁶⁷ Where a research exemption is not available, proceeding as if one exists likely facilitates the progress of research, but it relies on the hope that patent holders will not enforce their legal rights—a risky strategy.

Until better evidence of the actual impact of patents on research exists, and in light of the potential for patent infringement lawsuits, the risk that patents may slow or prevent research ought to be taken seriously. In countries without a statutory research exemption, or where such an exemption is very narrow, the promotion of patenting and licensing practices likely to promote widespread use of the invention is recommended. Other industries have managed to bring to the market products incorporating large numbers of patents, in part due to the willingness of patent holders to license their innovations under realistic terms.

III. Patents in the Treatment Context: Access to HIV/AIDS Drugs

Even more than in the research context, the impact of patents in the treatment context has generated considerable concern. The presence of patents has prevented the production of cheap drugs in some markets, and enabled high pricing, although it is also clear that patents and high prices are not the only—and often not the most significant—barrier to accessing treatment. Patented drugs for treatment of HIV/AIDS make an illustrative case, which brings into sharp focus the relationship between global intellectual property law, the market system, human rights, and health equity.

The extent of the HIV/AIDS problem is staggering. In the last two decades, over 30 million people have died of HIV/AIDS. According to a 2005 UNAIDS report, an estimated 40.3 million people are now living with HIV, with close to five million people becoming infected with the virus in 2005. Sub-Saharan Africa remains hardest-hit, and is now home to approximately 25.8 million people with HIV, almost one million more than in 2003. In fact, two-thirds of all people with HIV live in sub-Saharan

Government income in affected countries has declined because of negative economic growth. Available estimates suggest that HIV/AIDS has reduced the rate of growth of Africa's per capita income by 0.7 percentage points a year and that, for those African countries affected by malaria, growth was further lowered by 0.3 percentage points per year.⁷⁰ HIV/AIDS is also reversing important development gains at the very moment that governments need to increase their spending in the health care sector to deal with the disease, creating a financial and development crisis in the most affected countries. And the costs are not only financial in nature, but also social and psychological, with HIV/AIDS having a devastating effect on the social fabric of the affected countries.⁷¹

With proper administration, drugs can greatly prolong the lifespan of people with HIV/AIDS and reduce morbidity. The most beneficial drugs currently on the market are antiretrovirals (ARVs), which limit the damage that HIV does to the immune system and can prevent mother-to-child transmission.⁷² These are the most critical drugs

Until better evidence of the actual impact of patents on research exists, and in light of the potential for patent infringement lawsuits, the risk that patents may slow or prevent research ought to be taken seriously.

Africa, where an estimated 2.4 million people died of HIV-related illnesses in 2005. Outside Africa, the Caribbean (Haiti particularly), India, Russia, and China have the highest infection rates, and the epidemic is growing in Central Asia, East Asia, and Eastern Europe, where the number of people with HIV has increased by one quarter since 2003.⁶⁸

In Africa, socioeconomic factors and cultural traditions contribute to the spread and impact of AIDS, including the poor social status of women, widespread poverty, the collapse of public health systems, unemployment, rapid urbanization, wars, and the displacement of populations due to war and famine. It is not easy to quantify the economic impact of HIV/AIDS in African countries because the disease affects all sectors of the economy.⁶⁹ When the AIDS epidemic hit the worst-affected countries in the early 1980s, they were already struggling with development challenges, including debt and declining trade. But HIV/AIDS made a bad situation infinitely worse. Increased mortality has reduced the labor supply, and long periods of AIDS-related illness have reduced productivity in almost every sector.

because they reduce the viral load in the bloodstream to nearly undetectable levels and reduce opportunistic infections. In effect, they transform HIV/AIDS into a chronic infection requiring mostly outpatient care.⁷³ A combination or “cocktail” of antiretroviral drugs has thus far proven most effective. Anti-infective agents to treat or prevent opportunistic infections and palliative drugs to relieve physical and mental discomfort are also important, and most of them are available as affordable, generic drugs. All ARV medicines, on the other hand, are currently under patent in developed countries (although patents on three of the drugs will expire in 2006).⁷⁴ Currently, less than 5 percent of people in developing countries who need ARVs have access to them—and in sub-Saharan Africa, only about 1 percent have access. In North America and Western and Central Europe, a large majority of people who need antiretroviral treatment have access to it. As a result, AIDS deaths have stayed low since plummeting in the mid-to-late 1990s.⁷⁵ The role of patents in creating these access problems is by no means uniform, but as the following case shows, patent holders have legal rights

that they can use to prevent the production of cheap drugs.

Patents, Profits, and Patients: The Case of South Africa

In 1998, in what can only be called a disastrous public relations move, the pharmaceutical industry sought to prevent the government of South Africa from invoking a law intended to make essential medicines more affordable. Of particular concern were medicines for HIV/AIDS. At the time, over 4.5 million people in South Africa were infected with HIV/AIDS—the highest rate of HIV prevalence in the world—and thousands were dying each year.

The law sought, among other things, to allow generic substitution of patented brand-name drugs, promote competition in public drug procurement, improve drug quality, and make use of medicines more rational.⁷⁶ In its pleadings, the Pharmaceutical Manufacturers Association, representing thirty-nine pharmaceutical companies, argued that the law violated its members' property rights as guaranteed in the South African Constitution. The PMA also challenged the legality of the law's provisions regarding parallel importing and the discretion granted to the Minister of Health to grant compulsory licenses.

Internationally, supporters of the pharmaceutical industry argued that the actions of the South African government threatened the international patent regime enshrined in the multinational TRIPS agreement, and they sought to turn South Africa into a pariah state.⁷⁷ Initially this lobbying had some success, particularly in the United States, which placed South Africa on a U.S. Trade Representative watch list. A year later, however, South Africa was removed from the list as a result of pressure from an organized and global human rights campaign. Activists around the world pressured PMA to withdraw its claim by holding demonstrations and circulating petitions, including one signed by three hundred thousand individuals and one hundred forty groups from one hundred thirty nations.⁷⁸ By crafting their campaign as one of "patents and profits over poor African patients," international human rights activists were extremely successful in garnering support from the public and bringing the world's attention to the plight of impoverished Africans living with HIV/AIDS. In the midst of these global protests, major drug companies such as Merck cut drug prices in an effort to recoup some public support, blunt the offers from manufacturers of generic drugs, and stave off growing public discontent about patents on medicines.

Eventually PMA's case against the South African government became a major embarrassment for the pharmaceutical industry. In April 2001, three years after the case was filed, the drug companies withdrew it. The South African Minister of Health expressed his country's position this way: "We regard today's settlement as a victory in the sense that it restores to us the power to pursue policies

that we believe are critical to securing medicines at affordable rates and exercising wise control over them."⁷⁹ The government was thereafter free to implement its law and to import cheaper anti-AIDS drugs than those made and sold by international drug companies operating within South Africa.

The South African case brought increased international scrutiny to drug pricing practices in poor countries. Even though many drug companies initially argued that high prices for HIV/AIDS drugs were financially necessary, a good number began to lower their prices significantly in the face of fierce criticism from people living with HIV/AIDS, civil society organizations, and international human rights organizations. Since then, prices for AIDS drugs have dropped drastically in African countries—from approximately ten thousand dollars to less than two hundred dollars per patient per year. Offers by generic drug producers to provide cheap AIDS drugs have also pressured drug companies to reduce their prices.

Beyond these actions taken by pharmaceutical companies and generic drug producers to lower drug prices, the TRIPS agreement provided flexibilities for poor countries to increase access to essential drugs, including ARVs. A closer look at the specific TRIPS provisions is essential to understanding how these flexibilities play out in reality.⁸⁰

Clarifying the TRIPS Agreement: The Doha Declaration

There have been several difficulties in implementing the TRIPS agreement in the treatment context. Part of the problem lies in the interpretation of specific provisions intended to enable access to essential drugs, leading to further World Trade Organization council and ministerial meetings to clarify the language and the intention of the provisions. There have also been practical challenges, particularly for developing countries trying to utilize the agreement's flexibilities.

At the request of an alliance of African countries, the TRIPS council held two meetings in 2001 in Doha, Qatar, to discuss patents and access to essential drugs. Deliberations at these meetings centered on the objectives and principles of the TRIPS agreement (articles 7 & 8), the permissibility of parallel imports (article 6), and the use of compulsory licenses (article 31). A declaration was adopted that explicitly laid out the relationship between the TRIPS agreement and public health; it recognized the "gravity of the public health problems affecting many developing and least-developed countries, especially those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics," and acknowledged that intellectual property protection can affect drug pricing. Perhaps most importantly, the Doha declaration confirmed that "the TRIPS Agreement does not, and should not prevent members from taking measures to protect public health."⁸¹

In what can only be called a disastrous public relations move, the pharmaceutical industry sought to prevent the government of South Africa from invoking a law intended to make essential medicines more affordable. Of particular concern were medicines for HIV/AIDS.

Ordre public and commercial exploitation: Exceptions in patent law are permissible to prevent abusive commercial exploitation and to protect *ordre public*, morality, and human life or health. There is no universally accepted definition of *ordre public*; member countries have flexibility to interpret the exception in line with their social and cultural values. Arguably, however, *ordre public* is not limited to national security but extends to the protection of human, animal, or plant life or health and may be applied to inventions that may lead to serious prejudice to the environment.⁸²

Compulsory licensing: Compulsory licenses can be issued by governments for patented inventions if a proposed user has not succeeded, within a reasonable period of time, in negotiating a license directly with the patent holder.⁸³ Under the TRIPS agreement, the following conditions, among others, must be fulfilled before a compulsory license can be issued:⁸⁴

- The grantee must first have made efforts, for a reasonable time, to negotiate authorization from the right holder “on reasonable commercial terms and conditions.” Governments may dispense with this requirement in a “national emergency or other circumstances of extreme urgency or in the cases of public non-commercial use.”
- The use authorized by the compulsory license must be “predominantly for the supply of the domestic market.”
- Adequate remuneration must be paid to the patent holder.

The Doha declaration, while including a number of procedural conditions for granting compulsory licenses, made it clear that the TRIPS agreement does not limit the grounds on which compulsory licenses can be granted, and members have the right to stipulate such grounds in their own domestic laws.⁸⁵ It further reiterated the right of states “to determine what constitutes a national emergency or other circumstances of extreme urgency, it being understood that public health crises, including those relating to HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency or other circumstances of extreme urgency.”⁸⁶

Despite this positive development, the spirit of the Doha declaration in affirming the right to grant compulsory licenses is tempered by the reality that, as prices are forced down by compulsory licenses in developing countries, drug companies’ incentives to develop products for those markets are further weakened. This may occur in a research and development environment that already does little to establish products exclusively for developing world markets.⁸⁷

Parallel importing and other TRIPS issues: The Doha declaration reaffirms that member states may adopt legislation to allow parallel imports without the consent of the patent holder. It also exempts “least-developed countries” (as defined by the WTO) from providing patent protection to pharmaceutical products until January 1, 2016. Before this deadline, least-developed countries are free to increase their own capacity to manufacture generic drugs and to import cheap drugs from other member states.⁸⁸

Brazil and China both implemented laws recognizing product patents earlier than India, which meant that India was one of only a few countries that could legally produce generic versions of drugs patented after 1995. Nevertheless, India eventually had to become TRIPS compliant, and it created a system to accept patent applications for pharmaceutical products between 1995 and 2005.⁸⁹ Fortunately, all of the first-line ARVs were patented prior to 1995, and therefore the TRIPS agreement will not affect the generic production of these drugs in India; they can be used domestically and exported.⁹⁰ However, new drugs can be patented.

Finally, the Doha declaration urged developed nations to implement their TRIPS obligation to facilitate the transfer of technology to least-developed countries by providing incentives to local enterprises and institutes to promote such transfer.⁹¹

Manufacturing ability: The TRIPS agreement authorizes compulsory licenses predominantly for supply of domestic markets. Unfortunately, very few developing countries have well-established generic drug manufacturing industries, with the notable exceptions of India, which provides roughly 67 percent of pharmaceuticals for developing countries, and Brazil. The lack of manufacturing ability within developing countries was the unresolved issue at

the Doha conference, although it was clear that “members with insufficient or no manufacturing capacities in the pharmaceutical sector could face difficulties in making effective use of compulsory licensing under the TRIPS Agreement.”⁹² The ministers consequently requested that the TRIPS council find an “expeditious solution” to the problem.

Part of the problem was that developing countries wanted to import generic drugs produced in a third-party country under a compulsory license, but the third-party country’s ability to export those generic drugs was limited by article 31(f), which requires that production under compulsory licenses be “predominantly for the supply of the domestic market.” The term “predominantly” was not explicitly defined in the TRIPS agreement, but has generally been taken to mean that more than 50 percent of drugs produced under compulsory licenses should be intended for domestic consumption.⁹³

Many developing countries lack the technical skills to implement the provisions in the TRIPS agreement. The agreement and its accompanying declarations and decisions are exceedingly dense, and the interpretation requires considerable legal sophistication.

In August 2003, this problem was resolved—albeit controversially and only after long rounds of negotiations and compromise—by a decision adopted by the WTO’s general council. The decision is laden with administrative details and procedural requirements, but the core effect is to provide a waiver to the “predominantly for the domestic market” limitation. Any country with manufacturing capacity can now issue a compulsory license to produce generic drugs for export to countries that have insufficient or no manufacturing capacity, at least if various conditions are met.⁹⁴

Under the 2003 decision, importing countries can be least-developed countries, which are eligible to import without formal notification to the WTO, or any country that has committed to using these compulsory licenses only in situations of national emergency or extreme urgency (such countries have agreed not to use the system to lower the general cost of purchasing medicine for public health care).⁹⁵ All importing countries are required to take “reasonable measures within their means, proportionate to their administrative capacities and to the risk of trade diversion,” to prevent the reexport of the products they import,⁹⁶ a limitation that attempts to curb pharmaceutical arbitrage. Where a compulsory license is issued to serve an export market (as opposed to serving the domestic market), the exporting country, not the importing country, must pay compensation to the patent holder.

The decision also allows a recognized Regional Trade Area to be categorized as a single market under the TRIPS agreement provided 50 percent of its members are least-developed countries. An RTA is required to institute measures to safeguard against the risk of reexporting medicines destined for circulation in the RTA to prevent medicines destined for poor countries from being exported to developed countries. The advantage of an RTA is that it is a larger market than a single country and can therefore secure lower prices by purchasing in bulk.⁹⁷

There is little consensus on the practical effectiveness of the 2003 decision. Some believe that it shows that the WTO can handle humanitarian concerns alongside global trade issues, while others, mainly nongovernmental organizations, argue that the decision is so complex and riddled with restrictions, safeguards, practical hurdles, and red tape that it is unworkable.⁹⁸ How the decision will affect developing countries that rely on cheap Indian gener-

ic drugs is not clear. Efforts by poor countries to import generic drugs from India under the TRIPS provisions will depend almost entirely on the willingness of the Indian government to grant compulsory licenses and of Indian pharmaceutical companies to produce them.⁹⁹ Also, after India becomes TRIPS compliant, Indian pharmaceutical companies will have to license patented pharmaceutical products, and this may result in higher drug prices and internal competition among Indian drug companies; perhaps more importantly, the larger Indian companies will have to become innovator companies, developing their own research and development expertise in order to compete globally.

Political and Administrative Obstacles to Implementing the TRIPS Agreement

One of the issues that became clear during the lawsuit against South Africa was that many developing countries lack the technical skills to implement the provisions in the TRIPS agreement. The agreement and its accompanying declarations and decisions are exceedingly dense, and the interpretation requires considerable legal sophistication. Although there have been some efforts at building expertise and technical capacity among senior officials in the relevant ministries of developing countries, much more needs to be done for countries to gain the ob-

jective technical expertise to take advantage of TRIPS's flexibilities.

Also, developing countries themselves have to act strategically in order to make greater use of the TRIPS flexibilities. Policies to optimize TRIPS require an investment in human capital, an ability to attract capital, appropriate technology infrastructure, public support for technical progress and advanced scientific education programs, strong regulatory policies, and streamlined procurement policies.¹⁰⁰ Because TRIPS affects health, trade, law, and other administrative sectors, countries need to set up intergovernmental coordinating structures. At a minimum, working with TRIPS requires a certain amount of synergy and understanding among different sectors to devise efficient strategies for increasing access to essential drugs. Developing countries also need to show more of a political commitment by removing high-import tariffs for ARVs and essential medicine, particularly for donated drugs.¹⁰¹

Technical expertise is necessary but not sufficient. As observed in countries like South Africa and Brazil, attempts to exercise TRIPS flexibilities have met with pressure from pharmaceutical companies and the threat of economic sanctions from powerful WTO member countries.¹⁰² The United States, for instance, has already brought India and Brazil before the WTO in its efforts to seek stronger national patent laws and compliance with TRIPS. In another example, Thailand amended its Patent Act of 1979 to allow compulsory licensing and parallel importing in 1992. When Thailand began to produce a generic version of the HIV drug didanosine, an action that conflicted with U.S. interests, the United States—Thailand's biggest export market—threatened trade sanctions against Thailand. Under heavy pressure, Thailand stopped producing the drug and amended its laws to remove the clauses allowing for parallel importing and to limit compulsory licensing.¹⁰³ These threats have frustrated the efforts of developing countries to adopt national legislation that provides for compulsory licensing, parallel importing clauses, and other options in a manner most conducive for the health, economic, and development needs of their people.

Finally, although the TRIPS agreement lays out the minimum standards of intellectual protection required, there has been an increase in “TRIPS-Plus Free Trade

Agreements,” which undercut the flexibilities available under TRIPS. Some FTAs require that patent life be extended beyond the twenty-year TRIPS minimum, limit compulsory licensing, or limit the exception allowing for prompt importation of generics.¹⁰⁴ FTAs between the United States and Singapore and between the United States and Chile, for instance, set out higher standards of protection and enforcement for intellectual property in return for trade benefits.¹⁰⁵ TRIPS-plus clauses are also included in the controversial Free Trade Agreement of the Americas proposal.¹⁰⁶

Data Protection and Exclusive Marketing Rights

As a condition for registering pharmaceutical products, national authorities normally require registrants to submit data related to drugs' quality, safety, and efficacy, as well as information on the composition and the physical and chemical characteristics of the product.¹⁰⁷ When generic versions of a branded product are presented for registration, most regulatory authorities issue approvals based on the data provided by the original company, requiring only bioequivalence tests of the generic version. The TRIPS agreement obliges WTO members to treat such test data as a component of intellectual property. The rationale is that this rule permits the entity that generated the data to recover its costs, much as patents permit recovery of research and development investments. Protecting the data, it is assumed, provides private drug companies with the incentive to expend the considerable costs needed to produce it (although marketing approval, itself an incentive, often depends on the data).¹⁰⁸

According to Carlos Correa, an expert on TRIPS, data protection rules under TRIPS are potentially problematic for those developing countries that until recently did not provide patent protection for drugs (and to those still under the transitional periods of the TRIPS agreement). In these countries, there is a large pool of unpatented pharmaceutical products. If they provided exclusivity, data protection systems could become a partial substitute for patent protection in these cases, and they could in practice nullify the transitional periods granted to developing countries.¹⁰⁹

IV. Proposals for Change: Improving Access and Encouraging Innovation

Historically, patents have been considered a bargain between the individual inventor and society as a whole: in exchange for disclosing his or her invention to the public, the inventor is given a time-limited right to control who makes use of that invention.¹¹⁰ One justification for the time-limited right (the patent) is that it recognizes the inventor's reasonable claim that he or she has the "right" to profit from his or her creative labor. That the patent right is classified as a kind of property right significantly strengthens its legal standing. Indeed, E. Richard Gold and colleagues have argued that this classification has ethical consequences "because of a systematic bias in which property rights tend to trump all but the most compelling competing rights, including human rights."¹¹¹

Thus one can subject patents to a kind of rights-based analysis, where the impact of patent rights on other rights, including human rights, is considered. As described above, patents may in certain circumstances have an impact on health by affecting the price and availability of treatments and the progress of biomedical research. Although there has been some debate about whether health is a human right, the U.N. and WHO recognize it as a fundamental human right necessary for human flourishing and as pivotal for the exercise of other human rights.¹¹² A right to health is also supported by the philosophical principle of equality because without minimum levels of health, it can be argued, persons cannot meaningfully strive for equality.

When the promise of a patent encourages the creation of new treatments and technologies that improve health, patent rights may be compatible with health and equality—in fact, patent rights arguably even promote health and equality. On the other hand, once a technology or treatment exists, patent rights may be a major reason why those who need it can't afford it. That is, patent rights may then act as a barrier to improved health and improved equality, begging the question whether in such situations they ought to nevertheless trump those concerns. Once a new vaccine or drug or device exists, concern often shifts from providing incentives for the development of the innovation to ensuring that the innovation reaches those in need—at which stage the presence of patent rights can constrain access, depending on how they are exercised.

The bargain between disclosure and time-limited rights to control is also frequently justified on consequentialist grounds.¹¹³ Here the claim is that the promise of what may effectively be a short-term legal monopoly helps encourage innovation and attract the investment necessary "for large and expensive steps in scientific and technological research."¹¹⁴ An additional positive consequence that flows from issuing a patent is that a detailed description of the invention becomes part of the public record,

thereby advancing communal knowledge and providing the basis for improving it or incorporating it into new inventions.

Insofar as patents are justified on the basis of their expected positive consequences, they would appear unjustifiable if these intended positive outcomes do not result or if overall they generate more harm than good. Thus much research has sought to measure the impact of patents on the stated goal of innovation. But whether patents are necessary or sufficient to encourage innovation in biomedicine has proven difficult to measure.¹¹⁵ There are examples of countries that lack patent systems, or where patents are not available on particular kinds of biomedical invention. For example, until recently India would not issue patents on pharmaceuticals. History also contains examples of discoveries or inventions that were not patented, including by agreement of multiple inventors, as was the case when many single nucleotide polymorphisms (SNPs) were placed in the public domain by members of the SNP Consortium.¹¹⁶ Yet scholars caution against drawing sweeping conclusions from these specific examples about the impact of an absence of patents on biomedical innovation generally.¹¹⁷ There may be many reasons why the generic industry rather than original drug innovation flourished in India, and there may be many reasons why SNP research was able to progress without patents as an incentive or investment tool. Most likely, the impact of patents on innovation is mixed and highly dependent on other factors (including the presence of other incentives to innovate and other mechanisms to ensure affordability). Patents probably encourage biomedical innovation under certain circumstances (such as when the market is strong enough that the costs of developing, manufacturing, and distributing the product can be recovered), but they cannot reliably do so when many patented inventions are necessary for research to progress (especially if some of these are difficult to license) or when no reasonable market exists for any eventual product.

In addition to their impact on innovation, patents' impact on other social goods is also measured. Depending on one's philosophical framework, these "other social goods" might be understood as utilitarian goals or as rights. If we employ a utilitarian understanding and agree that the goals of law and policy are to improve the overall well-being of individuals and society as a whole, then the prospect that patents might lead to high prices and refusals of access to important medical innovations must be considered potentially problematic. The possibility of some harms would be acceptable, however, if they were generally outweighed by benefits.

One understanding of the patent system assumes that the benefits outweigh the harms. The U.K. Commission on Intellectual Property Rights makes this explicit:

The assumption is that in the longer run, consumers will be better off, in spite of the higher costs conferred by monopoly pricing, because the short term losses to consumers are more than offset by the value to them of the new inventions created through additional R&D.¹¹⁸

Yet as we have seen in biomedicine, the assumption that the patent system will yield a positive result even overall if some restrictions on access occur along the way is sometimes contested. To be clear: patents are not guaranteed to cause harms—much depends on the patenting and licensing practices of patent holders, the legal and political environment, and the wealth of the individual, institution, or jurisdiction in question. Moreover, even in the absence of patents, many problems persist. Yet in particular cases,

individuals to act in a certain way. Others rely on voluntary action.

Proposals to Improve Access and Facilitate Innovation

The proposals discussed below represent good faith efforts to avoid patents' harmful effects or to supplement their incentives for innovation. Some proposals seek changes in the law, while others seek policy changes or changes in practice. Not all these proposals will be adopted by all nations, organizations, or individuals, nor are they equally likely to succeed in their aims. Nevertheless, an awareness of these laws, policies, and practices, coupled with an expectation that the consequences for health will

When the promise of a patent encourages the creation of new treatments and technologies that improve health, patent rights may be compatible with health and equality. Once that treatment or technology exists, patent rights might help make it unaffordable.

the “short term losses” to which patents contribute can be serious, and in the context of individual human lives and particular research projects, those losses may not even seem to be short term.

Regardless of whether one sees patents as property rights “owed” to inventors or as a policy tool designed to encourage biomedical innovation and reward manufacture and distribution, at the very least one must acknowledge the possibility that property rights may clash with more important or fundamental rights, and that patents may fail to achieve their social goals. That is, we must see that the patent system does not guarantee that all needed innovation will occur, or that eventual innovations will be available to all those who need them to attain reasonable standards of health and well-being. One radical response to this possibility is to abolish the patent system altogether or to put all health-related inventions outside its reach. But this solution is unlikely to be adopted by any nation—in fact, the WTO has successfully persuaded countries to *extend* patent protection under the TRIPS agreement. A more moderate, realistic response maintains a patent system for biomedical inventions and supplements it with laws, policies, and practices designed to ease any patent-related access problems and to offer additional incentives to innovate where patents alone do not suffice.

Indeed, a number of measures have been proposed that essentially amount to this kind of “tinkering” with how and when patent rights are used in practice and in policy. Some of these measures are laws and treaties, like the TRIPS agreement, that require nations, organizations, or

be a priority for those in both public and private sectors, can go a long way toward facilitating important research and freeing up access to existing treatments.

Encouraging Innovation

The Medical Research and Development Treaty. The basic premise underlying the MRDT is that we need more than the patent system's promise of highly profitable sales to spur pharmaceutical research and development.¹¹⁹ The MRDT would establish a new framework for funding research for neglected diseases and act as a supplement to incentives offered by the patent system. It seeks to:

Create a new global framework for supporting medical research and development that is based upon equitable sharing of the costs of research and development, incentives to invest in useful research and development in the areas of need and public interest, and which recognizes human rights and the goal of all sharing in the benefits of scientific advancements.¹²⁰

Nations that sign the MRDT would shoulder an obligation to fund research in areas chosen by the treaty's governing body. Research funds would represent a percentage of gross national product, with other funds coming from market transactions such as purchases of medicine, philanthropic contributions, payment of royalties to patent holders, tax credits, innovation prizes, investments in competitive research mediators, and research and development obligations.¹²¹ The treaty would also adopt mecha-

nisms to limit patents on inventions developed through publicly funded research efforts.

The MRDT is an ambitious global effort aimed at closing the unacceptable research gap that currently exists between treatments aimed primarily at people who live in poor countries and those aimed mainly at people in developed nations. Much of the proposal assumes that government coordination of research and development will be fairer and more efficient than the current market system. There is, however, still no consensus on this question, and no hard evidence that this solution would work. In addition, given the vast social, political, and economic differences between the various signatory countries, building a consensus around the issues in the treaty will be difficult. A committee of eighteen experts is expected to meet twice a year to evaluate targets for priority research, make recommendations, and improve access to knowledge, technology, and other products. However, what criteria this committee will use in reaching consensus is not clear.

Finally, while the broad goals of the MRDT are important and necessary, much groundwork must be done to build the political buy-in needed to fulfill its essential elements. Several governments in developing countries have completely failed to give priority to their health care systems; they spend far more of their budgets on defense and other sectors.¹²² If developing countries spent more money strengthening their health care systems, this would improve the health of their citizenry both immediately and in the long term.¹²³ While these countries may not hesitate to sign such a treaty, it will be important for them to follow through, adhere to its terms, and meet their obligations, including providing a percentage of their country's gross national product to research, to ensure a sustainable source of income for the goals that the treaty lays out.

Advance purchase commitments. To deal specifically with the problem of few incentives in vaccine research, some analysts have proposed that governments, foundations, or international consortia make an advance commitment to purchase a certain quantity of vaccines at a certain price.¹²⁴ Such a commitment could take the form of a contract or binding agreement to buy from a prospective vaccine developer any new vaccine that meets specified criteria, including Food and Drug Administration approval.¹²⁵ Those sponsoring the deal could then pledge to make the vaccine available to poor countries at much lower prices.

The advance purchase commitment, which could be applied to vaccines and other target treatments, would provide a strong financial incentive to focus research and development in particular target areas that might otherwise not be financially attractive.¹²⁶ Critics of the proposal have argued that advance purchase commitments favor large pharmaceutical companies over small companies and nonprofit organizations.¹²⁷

Prizes for innovation. Prizes have been used since the early nineteenth century as an alternative to patents and government subsidies for providing an incentive to innovate. Oft-cited examples include Napoleon Bonaparte's offer of a prize to anyone who could find better ways to feed his troops, leading to the development of food canning, and the French government's prize for food preservation, leading to the discovery of how to prevent spoilage in glass bottles.¹²⁸ Prizes reward inventors only if their work succeeds, and they can spur only specific kinds of innovation—namely, innovation for which the desired outcome can be identified ahead of time.¹²⁹

Economist Michael Kremer and others have proposed prizes for pharmaceutical research on diseases that primarily affect the developing world. Kremer argues that such research could be encouraged by a public precommitment to buy desired innovations at a price that reflects their estimated social value.¹³⁰ Prizes would essentially be payments to innovators for the public's gains from their technology.

One of the challenges of this proposal is determining how large the prize ought to be. Historically, "prizes and rewards have been a small fraction of the social value of innovations."¹³¹ Kremer suggests a "patent buy-out" mechanism in which a prize amount is determined by the price at which firms would be willing to purchase the patent if it were for sale.¹³² A prize system that produces patent buy-outs would ideally place those patents in the public domain. Others have suggested that there should be a system of optional patent rewards under which governments could offer prizes greater than the patentee's monopoly profits, but smaller than the social value of the innovation.¹³³ Still others argue that governments should award prizes based on the profits obtained by a product in a test market.¹³⁴

Prizes are a viable alternative to patents in limited circumstances; however, there is not much consensus either on how research prize systems should work or on how or which international, government, or private agencies should administer the prize programs.¹³⁵ How the significant costs associated with the administration of prizes would be met in global, multi-institution research is also not clear.

The U.S. Congress is currently considering a research prize model. The U.S. Medical Innovation Prize Fund proposes allocating 0.5 percent of U.S. gross domestic product for rewarding innovative medical research. Under this program, a "winning" drug that receives approval from the FDA immediately becomes a generic, and the innovator is rewarded from the prize fund (spread out over the first ten years of the medicine's use) rather than by recouping costs through drug sales. The amount of prize money is linked to the relative therapeutic benefit of the new drug. Thus drugs for diseases that affect the poor primarily receive higher rewards, while "me-too" drugs with little new therapeutic benefit would be of lower priority.¹³⁶

The political philosopher Thomas Pogge has also developed a scheme of rewards under which inventors would have the option to forego the conventional patent for essential drugs and claim instead an alternative multi-year patent that would reward them out of public funding in proportion to the health impact of their invention.¹³⁷ Pogge argues that this alternative approach would spur drug development for neglected diseases that primarily affect the poor by providing financial incentives for drug companies to develop cost-effective interventions, since the reward would be contingent on the impact of their inventions in those markets rather than on the price they could charge. He proposes that such a plan would actually provide incentives for drug companies to sell their products cheaply, even below the production cost, so as to achieve health improvements among the very poor. The plan would allow the results of any successful effort to develop essential drugs to be provided freely, even to drug

local drug production in developing countries might appear to stimulate industrial policy and improve access, local manufacture of drugs might do little to ease access if the developing country has to purchase the raw materials (commonly referred to as “active pharmaceutical ingredients,” or APIs) from developed countries at high costs.¹³⁹ In the case of drugs to treat HIV/AIDS, producing APIs is expensive and requires a high level of expertise, and only a few companies do it. Since small or poor countries cannot produce their own APIs, they must compete with large pharmaceutical companies for them in the market.¹⁴⁰ They therefore must continue to import drugs and other treatment supplies that may be priced outside their reach.

Potential local manufacturers face several other problems, including a shortage of skilled labor, lack of PhD-level scientists, unreliable and excessively high-priced utilities, a weak financial sector, inflation, corruption, and

One proposed solution to the cost issue is to price the same treatment differently in different countries. Where it is technically feasible, this approach is ethical and economically sound and, applied along with other strategies, should greatly improve access to drugs in poor countries.

companies, as a public good. Pogge argues that this would allow for competition among manufacturing firms, and this would drive down the prices of drugs globally.

The proposal’s feasibility depends, of course, on the details, and these are still being worked out. Pogge concedes that the bulk of the funding for such a plan would have to come from the governments of rich countries, and the arguments justifying his approach would have to be persuasive from political, economic, and moral perspectives to gain any sort of traction.

Still others have proposed “pull mechanisms” under which vouchers are awarded for creating and licensing drugs that treat neglected diseases. To receive a “priority-review” voucher, the therapy would have to treat neglected diseases, receive approval by the FDA or European Agency for the Evaluation of Medicinal Products, be clinically superior to existing treatments, forgo patent rights, and find at least one manufacturer for the product. The awarded transferable voucher would entitle the bearer to orphan drug tax credits and priority review for another drug.¹³⁸

Lowering the Price of Patented Treatments

Local manufacture. A proposed solution to the cost issue is to manufacture drugs and devices locally. Yet as Warren Kaplan and Richard Laing have argued, although

weak legal, regulatory, and enforcement mechanisms, among others.¹⁴¹ These obstacles may greatly increase the cost of production. In fact, as Kaplan and Laing persuasively argue, it makes little economic sense for many developing countries to begin local production because economies of scale may be lost with the proliferation of production facilities.¹⁴²

Differential pricing. Another proposed solution to the cost issue is to price the same treatment differently in different countries. The classic theory of differential pricing (sometimes referred to as discriminatory pricing, tiered pricing, or equity pricing) is that “it is necessary to recover a substantial block of fixed costs (e.g. for research and development), by setting prices in a diversity of markets with differing demand elasticities.”¹⁴³ Differential drug pricing is a common practice in pharmaceutical markets. With the support of legal institutions, drug companies divide their markets along political and economic boundaries, offering price breaks to disadvantaged populations. GlaxoSmithKline’s best-selling combination ARV drug Combivir, for instance, costs approximately \$7,215 per year in the United States, whereas in sub-Saharan Africa, the drug is sold to health agencies for \$329 per year. It is not clear either here or in other cases what the true marginal manufacturing costs of patented drugs are—that information is hardly ever made public.¹⁴⁴

Several mechanisms designed to induce differential pricing in developing countries have been put forward by drug manufacturers, including voluntary price discounts and drug donations. Differences in price may also be due to diverse systems of government regulation and intervention, including government and institutional price controls and domestic IP legislation.¹⁴⁵

In the last decade there has been a sharp reduction in prices of HIV/AIDS drugs due to a variety of factors, including pressure from civil society (see the case against Nelson Mandela and the government of South Africa). In Brazil, threats of compulsory licensing have also led to a reduction in prices of ARV drugs for the Brazilian markets. Many pharmaceutical companies also have policies that specify which countries qualify for differential pricing for certain drugs. Unfortunately, in most voluntary differential pricing programs drugs are still more expensive than generics and are thus out of reach for many in developing countries.¹⁴⁶

One of the prime concerns drug companies have about differential pricing is “pharmaceutical arbitrage”—that is, the seepage of cheap drugs from poorer markets to rich markets. And over time, arbitrage erodes price-differentiated markets, moving all drug prices toward an equilibrium.¹⁴⁷ There are several ways to prevent this seepage, however. Examples include contracts that simply forbid arbitrage (with arrangements for compliance), product differentiation supported by trademarks, and the creation of appropriate regulatory structures.

Despite the potential for arbitrage, differential pricing schemes for drugs in developing countries are growing in popularity. The European Commission, for example, recently stated that differential pricing is the “principal means of rendering essential medicines affordable . . . to the poorest populations.”¹⁴⁸ The United Kingdom likewise supports a widespread commitment to differential pricing, as long as diversion of drugs to the EU markets is prevented through appropriate legislation and enforcement mechanisms.¹⁴⁹ Provided that differential pricing is technically feasible, it is ethical and economically sound and, when applied along with other possible solutions, should greatly improve access to drugs in poor countries. One way to ensure that differential pricing is at least considered is to make it a condition of research funding or include it as a condition in licensing agreements (see below).

Bulk and pooled purchasing. Another way of reducing the price of patented and unpatented treatments is through bulk purchasing, which can be used to leverage substantially reduced prices locally, regionally, and internationally. There are currently several international bulk purchasing initiatives for contraceptives, vaccines, tuberculosis drugs, and first-line ARVs. Organizations such as the Global Fund, Doctors Without Borders, The Clinton Foundation’s HIV/AIDS Initiative, and the World Health Organization help developing countries secure lower

prices by aggregating demand (that is, combining markets) and by obtaining advance purchase commitments that are credible, sufficiently financed, and that stipulate eligibility requirements and marketing exclusivity arrangements.¹⁵⁰

Bulk purchasing can have the effect of driving down drug prices by improving economies of scale, increasing the bargaining power of buyers, and reducing market asymmetries by sharing information between disparate purchasers. The Eastern Caribbean region has in recent years greatly increased access to drugs through regional bulk procurement and harmonization of essential medicine lists and regulatory systems. With the help of the Clinton Foundation, countries in that region have negotiated favorable ARV procurement deals with generic drug producers in India and South Africa, generating a savings of more than 60 percent on price currently paid by the Organization of Eastern Caribbean States.¹⁵¹

Limiting the Number of Patented Biomedical Inventions

Changes to patent law. Occasionally those worried about the effects of patenting call for changing national patent law, or the application of that law, in order to limit what can be patented. Two possible approaches include revising (and tightening) the patentability criteria and excluding certain inventions from patentability on moral grounds.

Certainly jurisdictions should periodically review both the laws that set out their patentability criteria and the operation of these laws. For example, new standards were released by the USPTO in 2001 in response to criticism of the utility requirement.¹⁵² In addition, as described above, scholars have called for better implementation of the legal patentability standards by U.S. patent examiners.¹⁵³ This might be achieved through more funding for the patent office and availability of stronger opposition procedures.

We have already noted that a jurisdiction can exclude some inventions from patentability under the TRIPS agreement, and that Europe has denied patents on this basis. But while one ought to take seriously the moral arguments against patenting certain kinds of inventions—including those involving human biological materials—these arguments do not resonate with all people at all times. That is, such exclusions may not be universalizable, and their applicability in a given jurisdiction may need to be revised and revisited on a regular basis as attitudes change (both for and against the exclusion). Because jurisdictions have the option to craft patent law that takes account of their moral concerns, and because moral concerns differ among as well as within cultures, morality-based exclusions ought to be respected and treated with sensitivity. Homogenous patent laws may facilitate international trade, but such homogeneity should not be at the expense of deeply held moral beliefs.

Those funding biomedical research can require specific patenting and licensing practices as conditions of funding. The existing legal system makes possible a variety of licensing strategies that different players can adopt to improve access and encourage innovation.

Changes to laws governing publicly funded research. Some legal reformers have called for restrictions on patenting by inventors whose research was funded using public monies (frequently academic researchers and their institutions). Arti Rai and Rebecca Eisenberg, among others, have called for specific changes to U.S. law so that federal funders have the power to restrict grantees' patenting and licensing activities (they can currently recommend certain practices but cannot make them a condition of funding).¹⁵⁴ This proposal seeks to reduce the discretion available to institutions as to how to handle their intellectual property. It is a direct response to the perception that profit rather than the public good has been the goal of academic technology transfer—a perception some academic technology transfer offices are seeking to change.

Electing not to patent. Patents are not international in nature. They apply only in those jurisdictions in which they have been filed and awarded. Individuals or organizations can therefore elect not to patent an invention or discovery at all, thereby dedicating it to the public realm; or they can decide to patent it only in some jurisdictions. The former strategy should be considered where inventions or discoveries do not require any further development to be useful, such as research tools that are ready for application. A decision not to patent sometimes follows from an agreement between researchers working on related work to make their findings available to each other and the public. Thus, for example, in the Human Genome Project and the SNP Consortium, agreements not to patent findings were adopted in advance. One term for this practice is “open source,” and it is an excellent way to make a collection of related inventions widely available. But this strategy may not always be financially desirable or feasible.

Individual inventors and their employers can also elect not to patent inventions in specific countries, thus leaving the market open in those jurisdictions for generic manufacturers.¹⁵⁵ This is a particularly attractive option for inventions used to treat diseases prevalent in both poor and rich countries. Revenue can be generated through patents filed in wealthy jurisdictions, leaving the invention patent free in the other jurisdictions. As an additional incentive, inventors are saved the costs of filing for and maintaining patents in multiple jurisdictions.

Companies that rely on revenue from inventions (even inventions ready for use and requiring no further development) to fund ongoing research might not be able to survive if they elected not to patent such inventions. The wisdom of not patenting will be a judgment, and we cannot ask companies to go bankrupt. But we can ask inventors and their employers to be honest with themselves about the reasons for patenting and the possible impact of patenting on more than profit.

Proposals to Make Patented Inventions More Widely Available

Legislating for a research exemption. A legislative option targeted at making patented inventions freely available for research would be to enact a research exemption. In the United States, there was some debate about whether an exemption to patent infringement existed at common law if the unauthorized use was for academic research. However, the absence of such an exemption was recently made clear in a court case (the United States has a specific statutory exemption for research leading to an FDA submission, but there is no general exemption for academic research).¹⁵⁶ The United States and other nations could choose to exact an exemption for specific kinds of research or research for specific purpose, although in the current biomedical research environment it may be difficult to draw clean lines between nonprofit and for-profit research. As the judges in the U.S. case pointed out, research is often a commercial activity even in academic institutions. Nevertheless, legislation creating circumscribed research exemptions remains an option for nations. Like any legislative reform of the patent system, it would need to be carefully thought out and would likely meet with considerable resistance. A similar effect can be obtained by including circumscribed research exemptions as licensing terms (see below).

Licensing practices and strategies. Electing not to patent at all or to patent only in certain jurisdictions can have an enormous impact on the availability of an invention for further research or therapy. But since patent holders may not always be able to clearly anticipate the end use of an invention, they may elect to patent in order to encourage further commercial development of an “embryonic” invention. Nevertheless, once an invention or

discovery is patented, they can use sophisticated licensing strategies to promote access and retain opportunities for research and development by organizations working in specific countries or on specific disease targets.

Too frequently, licenses are categorized as either exclusive or nonexclusive, depending on whether the patent was licensed to only one licensee or to many. But in light of the range of licenses and licensing terms now available, “simple reports on exclusive and nonexclusive licensing miss important nuances of licensing practice.”¹⁵⁷ In recognition of the potential impact of decisions made by individual inventors and their employers, those funding biomedical research can require specific patenting and licensing practices as conditions of funding. The existing legal system makes possible a variety of licensing strategies that different players can adopt to improve access and encourage innovation.

A recent tussle involving Yale University illustrates both the perils of not thinking things through and the opportunity for great social good when certain licensing strategies are employed, providing some hope that practices can change in the face of protest and convincing argument. Yale University is the patent holder for the AIDS drug stavudine, and Bristol-Myers Squibb had an exclusive license to sell the drug. Over the years, the partnership with BMS earned Yale profits of more than \$129 million. In 2000, Cipla (a drug manufacturer in India) and Doctors Without Borders requested a nonexclusive license from Yale and BMS to sell a generic version of stavudine, at a fraction of the cost, in South Africa. In the wake of pressure from Yale students, Doctors Without Borders, South African activists, and other humanitarian organizations, the university was able to renegotiate the license with BMS to permit the sale of the generics in South Africa. At the same time, BMS announced that it would lower the price of its brand-name stavudine to approximately \$55 per year throughout sub-Saharan Africa for governments and nongovernmental organizations.¹⁵⁸

Voluntary licensing arrangements for HIV/AIDS drugs—also known as humanitarian licensing strategies—are gaining popularity. In 2004, for instance, GlaxoSmith-Kline issued a voluntary license to South Africa’s Thembalami Pharmaceuticals to produce generic versions of two of GSK’s antiretroviral drugs—lamivudine and zidovudine. GSK has since issued more voluntary licenses for AIDS drugs in South Africa, Kenya, and India. This year, Bristol-Myers Squibb agreed to voluntarily license its new AIDS drug atazanavir to two generic drugs companies for reproduction—Emcure Pharmaceuticals Ltd. of India and Aspen PharmaCare of South Africa. Aspen PharmaCare is also producing generic versions of the ARVs Truvada and Viread under a voluntary licensing arrangement with Gilead. These companies will be allowed to set their own prices for the drugs to make them more affordable for developing world markets.¹⁵⁹

Limited exclusive licenses. A number of strategies have emerged that use limited exclusive licenses, including licenses that are exclusive to particular countries. Licenses might provide for exclusive use of the patented invention only in developed nations, or only in developing ones (some licensees may intend to develop an affordable or free medicine for the poor countries under an exclusive license limited to those countries). As Brewster and colleagues note, the challenges confronting this kind of “market segmentation” licensing strategy include the difficulty of containing products within the intended market¹⁶⁰ (although, as already discussed, this potential problem of arbitrage appears not to be as serious as once thought).

Licenses can also be exclusive to particular fields of use, which in effect means that they can be exclusively licensed multiple times for use in different kinds of research or product development. Where nonexclusive or limited exclusive licenses are issued, patent holders may retain the ability to license the invention or discovery to an organization, like a public-private partnership, that is seeking to develop a medicine or vaccine for a particular disease or an underserved or unprofitable market.¹⁶¹

Licensing to public-private partnerships. Because of the dearth of research into diseases that mostly affect poor countries, international health players—primarily philanthropic institutions, public agencies, and private sector developers—have begun entering into collaborative agreements to develop drug candidates for neglected diseases. There are an estimated sixty to eighty public-private partnerships (PPPs) in the global health arena. Examples of these partnerships include consortiums like the International AIDS Vaccine Initiative, Medicines for Malaria Venture, the Global Alliance for Tuberculosis Drug Development, and the Drugs for Neglected Diseases Initiative. These international joint ventures essentially reduce the developer’s risks and initial costs by subsidizing the research inputs, and they allow the donors to have greater control over product development.¹⁶² Because of the asymmetry of information between the donors and the private sector developers, it is not always possible for donors to determine which projects are the most promising and which costs are appropriate.¹⁶³ It is important, however, to point out that most PPPs recognize the basic validity of intellectual property rights, with some caveats, and this has made it easier for them to partner with drug companies.¹⁶⁴

While some partnerships aim essentially to ensure that research and development funding is available to battle diseases affecting poor countries, other partnerships—collectively known as product development partnerships (PDPs)—bring together within a single mechanism the work from various sectors that is crucial to the development of new health technologies. An example of a PDP is the International Partnership for Microbicides (IPM),

which was established in 2002 to accelerate the discovery, development, and accessibility of microbicides to prevent transmission of HIV. The IPM has entered into licensing agreements for the development of active compounds as potential microbicides with Merck, Bristol-Meyers Squibb, and Tibotec Pharmaceuticals, a subsidiary of Johnson & Johnson. Under separate agreements, each of these drug companies has granted to IPM a royalty-free license to develop, manufacture, and distribute their compounds for use as microbicides in developing countries.

According to a recent report of the Rockefeller Foundation (which provides a significant amount of funding for PDPs), these partnerships pursue accelerated product development and testing, as well as strategies to ensure access, using a clearly articulated business plan, and the management of a portfolio of candidate products.¹⁶⁵ The portfolio approach serves to insulate donors from risks inherent in selecting and funding individual candidate products. These PDPs use a business approach to bring

global norms and principals—each partnership sets its own rules, sometimes with little reference to a broader global public health framework. Some of the more powerful PPPs have been accused of redirecting national health policies and priorities, thus defeating or undermining local and national efforts. If countries with weak health systems institute PPPs, they could potentially fragment the health care system by creating independent, vertical programs that compete with the central system. PPPs and PDPs also have operational challenges, including ill-defined governance structures, imbalances in power and influence among partners, diverse motives and goals, and a lack of transparency and accountability.¹⁶⁸

Despite these problems, PPPs and PDPs have the potential to greatly narrow the research gap for neglected diseases, and they have the power to leverage broad private sector support (both domestically and internationally) for health development programs in poor countries. Patent holders should consider working with PPPs and

Commercial entities—particularly those in biomedicine—receive public assistance in the form of tax breaks, access to publicly funded research, access to markets and employees, and advocacy in international trade. These benefits arguably oblige a company to take public interest into account when making important patenting and licensing decisions.

new products for neglected diseases into the market as efficiently and cost-effectively as possible.

There are also partnerships to bring drugs already in the market to those who need them in developing countries. Pfizer, for instance, freely provides to fourteen African countries the antifungal drug Diflucan to treat two opportunistic infections—cryptococcal meningitis (CM) and oesophageal candidiasis (OC). These infections are estimated to occur in 10 to 40 percent of patients with advanced AIDS. Pfizer partners with ministries of health and other developing partners in those countries to ensure adequate support to successfully administer the program.¹⁶⁶ Likewise, the Merck Mectizan Donation Program works with public health agencies and nongovernmental organizations in poor countries to combat river blindness, the second leading cause of blindness in the world.¹⁶⁷

There are several problematic issues that PPPs and PDPs have to address, the most critical of which is financial sustainability. Some of these partnerships rely heavily on the good will of the private sector, and this makes for a particularly precarious situation with regard to the long-term fiscal health of the partnerships. PPPs and PDPs also suffer from a host of other problems, including a lack of

PDPs, and this work should include donating patented inventions and reserving the rights in license agreements to execute limited licenses to PPPs or PDPs.

Attaching conditions to licenses. As Brewster and colleagues note, conditions can be included in licenses that require the licensee to do certain things, such as “marketing a product in developing nations at a reduced royalty or price.”¹⁶⁹ They note that the U.S. NIH often includes these “white knight” clauses in its licenses to ensure that the licensee takes specific actions to benefit the public sector, including mandating supply-back of licensed products or services and creating a “worldwide development and marketing plan to facilitate developing country access to licensed products, implementation of which it monitors through agreed upon benchmarks.”

Licenses can also include performance milestones to ensure that the licensed technology is developed. As an example of such a license condition, Brewster et al. describe “a requirement that on or before the date of the first phase of a clinical trial for a new drug, the licensee will have identified a generic manufacturer in a middle-income country to produce the licensed technology at a reasonable price for developing countries.” In their survey, Press-

The biomedical industry deals in lifesaving or dramatically life-improving technologies. Its self-proclaimed role in society is to foster health. Responsibilities attaching to that honor could include the obligation to take account of the interests of those who are affected by its decisions.

man and colleagues found that one or more diligence milestones is included in approximately 80 percent of exclusive or limited exclusive licenses.¹⁷⁰

Retention of research rights. Finally, an increasingly popular condition in licenses is the retention of research rights. The Pressman survey found “evidence of a strong and expanding retained and transferable research-use right, even within exclusive, all fields of use licenses.”¹⁷¹ Brewster et al. suggest that patent holders “could insert a research exemption clause into licensing agreements that exempts specified categories and types of research from patent infringement.”¹⁷² Although a recent survey of over four hundred biomedical researchers in universities, government, and nonprofit research patent holders found little evidence of researchers altering or abandoning their research due to another’s patents, the study also noted that only 5 percent of researchers regularly checked whether their research might infringe a patent.¹⁷³ Explicitly including a research exemption is a prudent way to protect researchers, including researchers at other nonprofit research patent holders, from any possibility of legal challenge.

Among the drawbacks of all these new practices is the fact that they often require additional drafting and negotiating time. However, as new terms become more common, they will be easier to negotiate, and standard language will become available for easy inclusion in agreements.

Making Change in the Public and Private Sectors

A range of individuals and organizations play a role in patent policy and practice. International and national policy-makers are responsible for crafting treaties and laws that regulate patent rights, biomedical research, and drug delivery. National and international charitable organizations and national governments set funding policies and guidelines, which can require or recommend patenting and licensing practices. Individual and institutional patent holders—including nonprofit institutions, companies, and inventors—decide when and where to patent inventions. If they obtain a patent, they then negotiate with other individuals, institutions, or companies to determine who will access the invention and under what conditions. These different players exist for different reasons, are ac-

countable to different constituencies, and have different fundamental goals. Yet they have the ability to adopt one or more of the policies or practices described above.

The idea that some of these individuals and organizations should use their intellectual property to improve health and not simply to improve their own goals can be controversial. Although it is often accepted that the public sector (including governments and public universities) is under an obligation to consider the impact of patent rights on health of local and national communities (and perhaps even the health of people in other countries), the argument that companies are under similar moral obligations is less widely accepted.

Public sector. Public sector actors—governments, charities, and many nonprofit organizations and institutions—often explicitly try to benefit the public good. Universities, for example, may express a commitment to benefiting society in their missions and the missions of their technology transfer offices.¹⁷⁴ Obligations to benefit the public may also be inferred from their receipt of public monies, whether in the form of direct appropriations, grants, gifts, tax breaks, or other public assistance. Their patenting and licensing choices can therefore be assessed with reference to their missions, the stated goals of public funding, and any relevant laws or policies. The organizations that fund this public sector research—including the government, private charities and foundations, and individual donors—may be able to require certain patenting and licensing practices as conditions of funding (although in some cases that power may be limited by other policy and law).

Within the public sector, significant attention has focused on the policies and practices of universities, particularly in the United States, but increasingly in other countries. Although some academic institutions have always patented the results of some of their research, such patenting was not routine in the United States until after 1980, when legislation known as the Bayh-Dole Act encouraged the recipients of federal research funding, including academic research institutions, to patent the results of their research and license these inventions and discoveries to companies for further development.¹⁷⁵ This legislation has since been internationally influential.¹⁷⁶

As discussed above, controversies have erupted over universities’ patenting and licensing strategies when insti-

tutions have held patents on essential drugs and licensed them without provision for humanitarian use.¹⁷⁷ Similar access-based criticisms have been leveled at academic institutions holding patents on materials or inventions useful for ongoing research. In the case of treatments, it is argued that academic institutions have an obligation to the public good, which includes an obligation to improve health worldwide; in the case of research materials and process, the obligation can be expressed as a broad commitment to the pursuit of knowledge, which forms the basis for the norm of communism (or communalism) in science.¹⁷⁸ Perhaps because of these arguments, many academic institutions and technology transfer offices are working to adapt their patenting and licensing practices, as described above.

Private sector. Although generally considered to be focused primarily or even solely on generating profit for owners or shareholders, some scholars have argued that commercial entities should also seek to advance the public good.¹⁷⁹ In the case of health-related inventions, advancing health, promoting biomedical research, and generating a profit may go hand in hand. But even if they do not, researchers from the American Association for the Advancement of Science have argued that acting to advance health is unlikely to harm a company's bottom line in markets in which they do not operate or in which they do not make any money anyway (this argument relies on

being able to keep markets separate), and that “a corporation may advance its reputation for social responsibility and win greater esteem from the public” (and perhaps thereby win customers) by changing some of its patenting and licensing practices.¹⁸⁰

The argument can go further. There is an important analogy between private to public sector here. Commercial entities—particularly those in biomedicine—receive public assistance in the form of tax breaks, access to publicly funded research, access to markets and employees, and advocacy in international trade. These benefits arguably oblige a company to take public interest into account when making important patenting and licensing decisions (although such an obligation might be logically limited to the national or local “public” that has provided the assistance, rather than extending to individuals in other countries). In the case of the biomedical industry, the obligation is arguably heightened due to the very nature of their product. Unlike other companies, such as manufacturers of compact discs, the biomedical industry deals in lifesaving or dramatically life-improving technologies. Its self-proclaimed role in society is to foster health, and for that it has been long and justly honored.¹⁸¹ Responsibilities attaching to that honor could include the obligation to take account of the interests of stakeholders—those who are affected by the manufacturers' decisions—as well as shareholders.¹⁸²

Conclusion

In this report we have tried to contextualize the debate over the impact of patents on innovation and access in biomedical research and treatment. It is a context in which patents are only one of the forces spurring and rewarding research and development, and only one of the forces influencing who can access those innovations for more research and treatment. We have considered particular debates over patent rights on particular kinds of biomedical inventions, and we have canvassed some particular attempts to tinker with the existence and exercise of these rights.

Our conclusions are: (1) that patents are not always the optimal tool for encouraging biomedical innovation—indeed, they may sometimes be quite ineffective, and other policy tools may be required; (2) that the presence of patents on innovations useful in ongoing research make

wide ought to consider the possible impact of their biomedical patent rights on research and treatment and, if financially possible, consider actions that will facilitate access and promote ongoing innovation. Policy-makers should do what they can to facilitate and encourage such practices.

Although practice is generally voluntary (unless imposed as a funding condition or under institutional policy), it may well be the area in which the most dramatic changes can be achieved most quickly and with the most sensitivity to the particular context. Indeed, we suspect that changes in patenting and licensing practices—especially inclusion of research exemptions and limited exclusive licensing for humanitarian reasons—will dramatically reduce the impact of patents on access. Fortunately, such changes already appear to be taking place with the acade-

Patent rights should not always be treated as absolute, nor are they always the optimal policy tool to encourage innovation or to ensure access to biomedical inventions and discoveries.

may conducting that research difficult, but generally only when those controlling the patent rights do not seek to make their innovations widely available; and (3) that the presence of patents can be a key reason that biomedical treatments (and vaccines) are too expensive for some of the world's populations, but that the absence of patents alone is not enough to guarantee access. Finally, we conclude (4) that creative and targeted policies can and should be used to encourage innovation not sufficiently encouraged by the presence of the patent system alone, and (5) that as long as a patent system persists (and we are not suggesting that it be abolished), developing sophisticated patenting and licensing practices that are sensitive to potential access problems, particularly if resolving those problems could greatly improve the lives of the world's poor and sick, is key to improving the biomedical research and treatment systems.

Given the importance of biomedical research and biomedical treatments to the fundamentally important social goods of health and equality, patents should not always be treated as absolute property rights by those who control them. At a minimum, public and private actors world-

mic technology transfer community.¹⁸³ To that end, greater awareness of the consequences of patent laws and policies—especially policies aimed at improving access for research and treatment realistic expectations about the profitability of patents and licenses, responsiveness to changing situations, and a shared view of the importance of access for health and well-being—will be key. Without awareness, realistic expectations, a willingness to be responsive, and a shared belief in the importance of promoting health, changes in common practice (let alone in law and policy) will not be possible.

Generating new inventions and discoveries that address important health problems and making existing inventions and discoveries available to those in need are important policy goals that lawmakers, policy-makers, research funders, and those controlling patent rights should bear in mind. Health-related patent rights should not always be treated as absolute by the individuals and organizations controlling them. Nor are they always the optimal policy tool to encourage innovation or to ensure widespread access to biomedical inventions and discoveries.

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Patents: A Glossary

Patents: legally enforceable property rights issued by regional patent offices to inventors, allowing them to control who may make and use their invention or discovery. When the patent expires the invention is “off patent.”

Licenses: permission from the patent holder to make or use a patented invention, usually in exchange for a fee.

Generics: pharmaceutical products—drugs and vaccines—that are exact copies of patented products but are produced without a license from the patent holder.

Parallel imports: importing a patented invention into a jurisdiction in which that invention is already sold.

Compulsory licenses: allows a government to declare that it or an identified other may manufacture, use, or import a patented invention without the patent holder’s permission. Patent holders are usually entitled to “reasonable compensation.”

Differential pricing: also known as tiered pricing or preferential, means that different classes of buyers are charged different prices for the same product.

Exclusive license: a license specifying that only the licensee may make and use the patented invention (that is, the patent holder agrees not to issue any other licenses).

TRIPS agreement: Agreement on Trade-Related Aspects of Intellectual Property signed by members of the World Trade Organization (WTO) in 1995.

DOHA declaration: a WTO declaration of 2001 that clarified the TRIPS agreement’s provisions concerning the flexibility of intellectual property rights in the face of public health concerns.

Pharmaceutical arbitrage: arbitrage occurs when drugs sold cheaply in poor countries under differential pricing schemes find their way into richer markets where identical drugs are sold for much more.

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