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Articles

*1031 ADDRESSING GLOBAL HEALTH INEQUITIES: AN OPEN LICENSING APPROACH FOR UNIVERSITY INNOVATIONS

Amy Kapczynski [FNd1]

Samantha Chaifetz [FNdd1]

Zachary Katz [FNddd1]

Yochai Benkler [FNdddd1]

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***1032** I. INTRODUCTION

Each year, millions of people in low- and middle-income (LMI) countries die from preventable and treatable diseases. [FN1] AIDS provides one of the starkest examples: it killed more than three million people in 2004 [FN2] and has become the world's leading cause of death for adults aged fifteen to fifty-nine. [FN3] These deaths continue despite the fact that we have known for years that antiretroviral combination therapy (ARVs) can substantially improve the lives of those living with HIV/AIDS, and even reverse the tide of death associated with the disease. [FN4]

But the drugs that we take for granted in the United States have long been out of reach for most of those living with HIV/AIDS around the ***1033** world. [FN5] One crucial reason has been their cost. In 2000, the average worldwide price for patented ARVs was more than $10,000 per patient per year. [FN6] Today, the same medicine is sold in generic form for as little as $168 per year. [FN7] This drastic reduction in price has enabled governments and international agencies to initiate programs designed to bring these medicines to millions of HIV-positive individuals around the world who otherwise lack access to them. [FN8] These programs still have a long way to go before they meet existing need, [FN9] but they would not have begun at all if prices had not come down so dramatically.

***1034** These recent price reductions have also generated a storm of controversy regarding the contribution that patents and other exclusive rights [FN10] make to the inequities in global availability of life-saving medicines. The problem that patents can pose for access to medicines and medical technologies [FN11] is complex and cannot be understood without a nuanced assessment of the political economy in which the key players operate.

Consider one example: in 2000, only an estimated one percent of the 500,000 South Africans in need of ARV medicines received them. [FN12] The humanitarian organization Médecins Sans Frontières (MSF), better known in the United States as Doctors Without Borders, wanted to begin a pilot program in a township outside Cape Town to demonstrate that, contrary to popular belief (and the claims of South African President Thabo Mbeki [FN13]), AIDS medicines could be used effectively in resource-poor settings if they could be made affordable. [FN14] MSF faced a practical problem: a limited budget and a seemingly unlimited supply of patients. In South Africa, the price of stavudine, just one of the drugs then used in ARV therapy, was over $1600 per year. [FN15] An Indian company offered to sell MSF generic stavudine for approximately three percent of the branded version's price, ***1035** but because the drug was subject to a South African patent, MSF could not legally accept the offer. [FN16]

Though Bristol-Myers Squibb (BMS) had an exclusive license to sell the drug, Yale University was the key patent holder. [FN17] MSF approached Yale in February 2001, requesting a license to use generic stavudine. MSF simultaneously asked BMS for a price reduction that would lower the price to the generic level. [FN18] In addition to its immediate, pragmatic objectives regarding its pilot program, MSF likely also had a broad strategic goal in mind. At that time, patent-based pharmaceutical firms [FN19] refused to offer transparent and comprehensive price reductions for AIDS drugs for developing countries, [FN20] threatened to sue generic companies that supplied ARVs to developing countries where the firms believed they held patents, [FN21] and sued the South African government over a statute intended to allow cheaper medicines into the country. [FN22] MSF no doubt hoped that Yale would act differently than the drug com-

panies, setting a precedent that would ultimately demonstrate that, contrary to drug company assertions, price discounts and patent concessions in countries like South Africa would not destroy the patent-based pharmaceutical industry. [FN23]

***1036** This approach paid off. Within weeks of receiving MSF's request, Yale and BMS jointly announced that they would permit the sale of generics in South Africa and that BMS would lower the price of its brand-name stavudine to approximately $55 per year throughout sub-Saharan Africa for governments and nongovernmental organizations (NGOs). [FN24]

The Yale/BMS decision garnered significant media attention, [FN25] and may have helped create a tipping point in the campaign for access to affordable ARVs--shortly after the announcement, pharmaceutical manufacturers dropped their lawsuit against the South African government. [FN26] Major price reductions in sub-Saharan Africa followed from other companies, [FN27] as well as additional concessions on intellectual property rights (IPRs). [FN28] This in turn enabled activists in countries such as South Africa to turn the spotlight on their own government's inaction, and eventually obtain commitments to provide ARVs in the public sector. [FN29]

***1037** In renouncing the enforcement of its South African patent, Yale went further in making intellectual property (IP) concessions on an AIDS medicine than any proprietor had done before, and demonstrated that patent holders could trigger substantial, immediate price reductions. The Yale/BMS deal may also have been a watershed event for public sector institutions (which we define as public and private universities, governmental agencies, and nonprofit organizations). Over the past few years some such institutions have taken steps to ensure that their patents do not contribute to what we call the “access gap”--the systematic inability of individuals in developing countries to obtain existing medicines.

Public sector institutions have also begun to address a related problem--one we term the “research and development gap” (R&D gap)--of massive underinvestment in medicines for diseases that primarily impact the global poor, known as neglected diseases. [FN30] The scale of the inequality is immense: “only 10% of the world expenditure on health R&D is spent on health conditions that represent 90% of the global [disease] burden . . . .” [FN31] Although the R&D gap has received far less attention than the access gap, its implications are no less grim.

Consider one vivid example: the most commonly used drug to treat African sleeping sickness is arsenic-based and kills up to five percent of ***1038** those who are treated with it. [FN32] New drugs are desperately needed for this and many other diseases, but have not been forthcoming. Of the many reasons for this, the most important is that our current drug development system primarily depends on patents (and their corresponding market-based incentives) to draw private companies to fund clinical trials and commercialization activities. Predictably, firms have little interest in developing products for developing countries because these markets are so small: the branded pharmaceutical industry in the United States derives only five to seven percent of its profits from all LMI countries. [FN33] Indeed, Latin America, Africa, Asia (excluding Japan), and Australia combined comprise only twelve percent of the total worldwide market for pharmaceuticals, including generic drugs. [FN34]

***1039** While patents--and the promise of exclusivity--alone cannot stimulate research where there is no attractive market for a medicine, they can create barriers to such research, and thus play a role in perpetuating the R&D gap. Public sector institutions are beginning to address both the need to stimulate research and to ensure patents do not block research, for example, by participating in public-private partnerships to develop medicines for neglected diseases and by seeking to reserve rights to use one another's research tools.

This Article aims to draw upon these examples to demonstrate the potential of public sector institutions, particularly U.S. universities, [FN35] to address the access and R&D gaps by changing their licensing practices. It also aims to pro-

pose a strategy that will allow these institutions to settle on a standard practice that will best use their collective contribution to innovation. We demonstrate that without any changes in the current statutory or regulatory environment, these institutions can use private, contractual instruments to foster commons-based remedies for the problems of our global drug development and distribution system. This Article outlines the structure and characteristics of two such instruments to: (1) eliminate the access barriers exclusive rights pose to patients in LMI countries, and (2) remove patent barriers that might impede research on neglected diseases.

These strategies will only be effective if they are rooted in an understanding of the role that IPRs play in the access and R&D gaps. Part II provides such an analysis and argues that patents and other exclusive rights regimes are now an essential subject for anyone concerned with global health disparities. We also review existing proposals to eliminate the burdens patents can impose on the global poor, and demonstrate the acute need for new approaches--particularly ones that can route around the inaction of governments and firms, and have a demonstration effect that will prompt systemic change.

Part III seeks to define the space from which such an approach can emerge. We discuss a class of commons-based initiatives that provide a model for action that depends neither on top-down governmental action, nor on private market motives and signals. [FN36] Commons and common-property regimes in material resources have been the subject of substantial ***1040** scholarship over the past two decades. [FN37] The emergence of free and open source software development has led to increased interest in defining the conditions for sustainable and successful nonproprietary production strategies--for software [FN38] and more generally for networked information production [FN39] and some classes of physical resources. [FN40] These approaches rely on mechanisms other than proprietary exclusion to motivate and to organize production, and they frequently rely upon innovative contractual provisions to create a self-perpetuating commons. In this Part, we discuss recent, exploratory public-sector projects that implement commons-based approaches within the biomedical domain, as well as the models and lessons these projects can take from other commons-based, contractually structured initiatives.

In Part IV, we analyze the current structure of university research and technology commercialization, demonstrating that U.S. research universities are well-positioned to adopt open licensing policies [FN41] that could meaningfully benefit the global poor. This Part explains the role of universities in the overall biomedical innovation system and discusses the problems with their standard approach to patenting and licensing biomedical innovations. We also map the political economy of a move towards open licensing within universities, demonstrating that such licensing is not contrary to the financial interests of universities, and may in fact provide substantial gains for universities as well as the global poor. The success of this proposal***1041** will depend on its adoption by a critical mass of research universities.

In Part V, we propose two open licensing models that universities (and other institutions) can adopt to improve access to biomedical innovations in LMI countries. We call the first approach Equitable Access ("EA") Licensing. The approach relies on including EA clauses in the technology transfer licenses universities negotiate with drug companies engaged in commercializing the universities' academic discoveries. The EA provisions we propose give third parties--for example, manufacturers of generic medicines--freedom to operate in LMI countries with regard to the licensed technology or any derivative products, by adapting the so-called "copyleft" characteristics of some open source licenses. [FN42] EA clauses also establish a self-enforcing open licensing regime that minimizes transaction costs and is insulated from the vicissitudes of internal university politics and market relationships.

We refer to the second open licensing approach as Neglected Disease ("ND") Licensing. Like EA licensing, ND licensing is a commons-based strategy. ND clauses are designed to provide those engaged in neglected disease research the freedom to experiment on and with proprietary university technologies. Furthermore, ND clauses allow researchers to

freely market, in LMI countries, any innovations without hindrance from exclusive rights held by the university.

One of the lessons of our analysis of various licensing provisions is that there is no one-size-fits-all commons-based strategy. Different strategies to create and sustain commons-based production in different contexts may be required by: different economic characteristics of research areas; different industrial structures and relative roles of market-based, governmental, and nonprofit enterprises; and different types of exclusive rights regimes.

Our proposal is deliberately modest. We suggest an intervention in the existing industrial structure of the research, development, manufacture, and distribution of curative and preventive treatments. But the intervention we advocate is not aimed at fundamentally restructuring these fields. Instead, we suggest taking advantage of the existing distribution of firms and ***1042** business models, the relatively large role of public sector institutions, and the distribution of needs, wealth, and markets. Our proposal is intended to complement, rather than displace, current proposals to reorganize the market for drug development through top-down legislative change. The shift we describe provides a way for organizations and firms to take immediate steps to positively affect the lives of patients in LMI countries, and perhaps to catalyze broader action to promote global health.

II. HOW PATENTS AND OTHER EXCLUSIVE RIGHTS AFFECT THE GLOBAL ACCESS AND R&D GAPS

A. Innovation Theory and the Second Enclosure Movement

The past two decades have witnessed a steady, global trend toward ever more restrictive patent and related exclusive rights regimes, dubbed the “second enclosure movement.” [FN43] In the United States, for example, the scope of patentability has expanded to include bioengineered organisms and purified genetic material, [FN44] and “early ‘upstream’ inventions that explain disease pathways and mechanisms and identify potential drug targets are increasingly likely to be patented.” [FN45] Patents have also been increasingly supplemented with exclusivity offered at the drug regulatory interface. [FN46] Over the same period, the United States, the European Union, and Japan have used trade agreements to impose high levels of substantive and procedural protection for IP on countries around the world. The World ***1043** Trade Organization's (WTO) Trade Related Aspects of Intellectual Property (TRIPS) Agreement is the foundation of this treaty architecture, [FN47] but regional and bilateral agreements increasingly impose even higher protections upon countries. [FN48] This shift towards stronger IP protection--driven by the lobbying power of Hollywood, the recording industry, prepackaged software companies, book publishers, and pharmaceutical companies [FN49]--represents a massive and unprecedented experiment in innovation policy. This is particularly true in the area of medicine: at the time the Uruguay ***1044** Round of trade negotiations was launched, more than fifty countries did not provide patent protection on medicines. [FN50]

Proponents of this IP expansion contend that it will spur innovation and therefore increase aggregate social welfare. This reflects the dominant justification for patents and other forms of IP. In wealthy economies (even where the copyright tradition is premised upon moral rights), these rights are consistently cast in utilitarian terms: the rights are considered first and foremost a tool to encourage private investment in information goods. [FN51]

Economists, however, are ambivalent about the effect of strong exclusive rights on innovation and welfare. [FN52] This stems from the fact that information is both nonrival and a critical input for further innovation. Once produced, information--such as a scientific formula--is most efficiently accessible at its marginal cost of zero. If priced at zero, however, firms will not invest in research. Patents are one solution to this; they incentivize innovation by granting firms

a temporary monopoly period in which to reap supra-marginal profits. But they also create deadweight loss by raising the marginal cost of consumption above zero. Such exclusive rights also have the potential to stymie innovation because information is a component in its own production. Patents thus raise the costs of innovation, even as they increase its potential value. As a result, even in a dynamic analysis, an overly expansive set of rights leads to too little innovation. [FN53] Strong patents--particularly in the aggregate--have been shown, both theoretically and empirically, to reduce both innovation and welfare. [FN54]

***1045** Many who accept these premises nonetheless consider the pharmaceutical sector an exception. [FN55] They argue that the industry is distinguished by its relatively high cost of R&D and relatively low cost of reverse engineering, and they point to survey data that suggest that patents are central to pharmaceutical firms' appropriation strategies. [FN56] But all that these facts show, respectively, is that some mechanism is necessary to promote innovation in this sector, and that those firms that dominate under the current system are dependent upon the tools that brought them to dominance. Economists have long debated whether direct government funding or prize systems would have better welfare effects than patents. [FN57] Calls for alternative strategies to incentivize pharmaceutical development have grown more marked recently, supported by claims that the current pharmaceutical market misdirects innovation and marketing resources, leads to inefficiently high prices, and promotes both counterfeiting and price controls. [FN58]

Importantly, all of these general conclusions are premised (if only implicitly) on the experiences of wealthy countries and on a one-country model of the market for innovation. When we consider the particular context***1046** of developing countries, we find that patents will cost them significantly more, and benefit them significantly less. In the Section that follows, we make this case and relate it to the existing global crises around access to medicines and R&D for neglected diseases. We demonstrate that exclusive rights can be an important cause of unaffordable pricing of existing medicines in LMI countries and can also create impediments to R&D for neglected diseases.

B. The Access Gap and Exclusive Rights

According to the World Health Organization (WHO), roughly ten million lives around the world could be saved every year by improving access to essential medicines and vaccines that already exist. [FN59] Approximately thirty percent of people around the world do not have regular access to essential medicines, and "in the poorest parts of Africa and Asia this figure rises to over 50%." [FN60] This is what we term the "access gap," and it has many determinants. [FN61]

***1047** One important determinant is price. [FN62] Unsurprisingly, there is "considerable evidence that consumption of medicines is sensitive to price." [FN63] In particular, price has disproportionately severe effects on patients in LMI countries. [FN64] Not only are consumers in these countries poorer on average, ***1048** but they also tend to pay a greater proportion of their own medical costs than consumers in wealthy countries. While patients in wealthy countries are often insulated from the high cost of medicines by third party payers (for example, insurance companies or government funded programs), in LMI countries, "public medicine expenditure does not cover the basic medicine needs of the majority of the population" [FN65] and private health insurance is rare. [FN66] In both low- and middle-income countries, the public sector pays less than thirty percent of drug costs. [FN67]

Price, in turn, is affected by patent status. Empirical studies focused on developing countries predict, for example, that "the introduction of patent regimes . . . has, or is predicted to have, the effect of raising prices. The estimates range widely depending on the drugs and countries being considered-- from 12% to over 200%, but even the lower estimates imply very substantial costs for consumers." [FN68] Development and aid agencies working in the field confirm these theoretical predictions. MSF has concluded that "[t]he most significant factor in lowering prices [is] the introduction of generic sources in a country," [FN69] and Oxfam International has ***1049** called generic competition the single most im-

portant tool to remedy the access gap. [FN70]

Some have argued that pharmaceutical companies are unlikely to patent in LMI countries, and therefore that we ought not focus on patents as a barrier to access. [FN71] This position has been widely discredited based on evidence of patenting, particularly in key supplier markets. [FN72] Pharmaceutical companies have been willing to patent widely, and cling to the exclusivity that their patents provide, even where the public health implications are dire. [FN73] And although, as we might expect, gross national income, market size, and relative income inequality are generally important determinants of patenting strategy, [FN74] patenting still occurs in low-income countries. [FN75]

Furthermore, the absence of patents in a given country is not the sine qua non of effective access to generics. A supply of medicines must also exist, but "[d]eveloping countries differ substantially in terms of their existing pharmaceutical production capacity." [FN76] In the poorest countries, ***1050** even when medicines are locally formulated, they may be unaffordable because of inefficiencies in production and limited market size. [FN77] As a result, patents in a variety of countries can matter a great deal to the shape of the supply curve. Patents may obstruct production and export from certain countries, namely middle-income supplier countries--such as India--which play a critical role in the global market for generics. They may also limit the available markets to those that are too small to justify the costs of reverse engineering specific medicines, retooling production facilities to make them, or establishing distribution networks. For example, while many poor and low-prevalence countries in Africa have few or no patents on ARV medicines, it was not until late 2003 that the first African company began to locally produce ARVs. [FN78] As one would expect, that company is based in South Africa (where, not incidentally, patents first had to be overcome). [FN79]

While patents are not the only factor blocking access to medicines, exclusive rights in one LMI country can create serious, preliminary obstacles to access in that country and prevent the emergence of a competitive market to supply medicines to another country that has no such barriers. Finally, the aspects of this problem that are visible today are only the tip of the iceberg. It is easy, but shortsighted, to ignore the value of medicines that have not yet been developed. [FN80] Obviously we expect--and need--new medicines. As they come into being, as TRIPS takes hold in supplier countries***1051** such as India, and as TRIPS-plus provisions take effect in more and more countries, the role of exclusive rights in the access crisis will grow more important. Though sobering, this is only half of the problem.

C. The R&D Gap and Exclusive Rights

1. The 10/90 Gap

Significant morbidity and mortality in developing countries result from diseases for which there are currently no effective, easy-to-use medicines. [FN81] Unfortunately, our patent-based R&D system does not adequately address this problem. A mere ten percent of the world's expenditure on R&D is devoted to conditions that cause ninety percent of the global disease burden--a situation that has been termed the "10/90 gap." [FN82] Only one percent of medications introduced between 1975 and 1999--thirteen out of an estimated 1393--targeted tuberculosis and tropical diseases (including malaria and infectious diarrhoeal diseases) which cause 11.4% of the global disease burden, including a substantial proportion of the disease burden in developing countries. [FN83]

Beyond the gap in development, the current system fails to optimize existing medicines and medical technologies for use in developing countries. For instance, heat stable formulations--essential in countries with warm climates and little refrigeration--do not exist for several essential medicines, such as insulin and oxytocin. [FN84] Many desirable fixed-dose ***1052** combinations, which combine several medicines into a single pill and make prescribing and adhering to complex medical regimens much simpler, do not exist. [FN85] Diagnostic and monitoring tools developed for high-income

markets are often inappropriate for use in developing countries and may cost more to use than the medicines involved in treating the underlying illness. [FN86] We also lack formulations for small patient populations with special needs, such as children, particularly where most patients live in developing countries. [FN87]

As Juan Rovira, a former Senior Health Economist at the World Bank, has observed, "the patent system leads R&D toward profitable diseases and conditions, rather than toward diseases that cause the most morbidity and mortality." [FN88] Thus, just as the static costs imposed by patents cannot be understood in a hypothetical one-country model, neither can the potential dynamic effects of patents. The dynamic benefits of patents for poor countries are likely to be much smaller than the one-country model predicts, because their markets are small compared to those markets that already offer patent protection. [FN89] Under the circumstances, it is not surprising that pharmaceutical companies do not direct their research towards these markets. [FN90]

***1053** 2. Patents As Barriers to R&D, Particularly for Low-Commercial-Value Research

The R&D gap is perhaps the most obvious manifestation of the dynamic failures of patents for people living in LMI countries. Simply put, patents do not help the poorest of the poor because a monopoly in such a market is worth very little. But as noted above, patents can also create a drag on the innovation process itself; this can be particularly problematic where the research in question has low commercial value.

As the number of patents and patent holders associated with a given biomedical innovation increases, [FN91] so do the transaction costs associated with conducting research. These costs are at the center of recent concerns about the growth of an "anticommons" [FN92] or "patent thickets." [FN93] The need to negotiate permission to use or litigate disagreements about research tools slows research and increases its cost. [FN94] While transaction costs only rarely completely prohibit commercially valuable research, [FN95] they may hinder research at universities or nonprofit institutions concerned with developing world diseases where commercial pay-offs are at best uncertain. [FN96] Indeed, several of the concrete examples we have of patent thickets ***1054** that have caused lengthy delays, or of broad and exclusively licensed research tool patents that have obstructed research initiatives, relate to products intended for developing countries. [FN97]

There is also evidence that patents cause scientists to redirect their research efforts towards "areas with more intellectual property freedom." [FN98] Such redirected research may be less efficient or successful, particularly if the areas most crowded with patents are also those that scientists deem most promising. Patenting practices may also dampen scientific exchange. Recent data suggest that university-based geneticists who engage in commercial research are more likely than their peers to withhold data from fellow academic scientists. [FN99]

More broadly, patents give their owners the right to block research outright. [FN100] A few patents on an important gene target, for example, have ***1055** the potential to slow research for a generation. [FN101] A firm may want to block other researchers for a variety of reasons, including preventing competitors from gaining an advantage and retaining all of the potential value of improvements for itself. [FN102] Pharmaceutical firms are particularly reluctant to allow research on therapeutic compounds, citing two concerns: (1) the possibility of being excluded from future developments of their products, and (2) the possibility that the researcher will "generat[e] and disclos[e] data that could create problems for the firm in seeking FDA approval." [FN103]

Unlike companies, universities may be willing to license the research tools they develop freely to other public sector institutions. In practice, though, they sometimes grant exclusive licenses to companies that then refuse to sublicense any rights or that impose onerous terms on sublicensees. [FN104] Recent research suggests that public institutions may issue such exclusive licenses with alarming frequency, even where the tools are useful primarily for diseases prevalent in de-

veloping countries. For example, a recent map of patents relevant to the development of a malaria vaccine found that only eight of the twenty-seven "moderate to high priority" patent***1056** families that were originally filed by public entities remain available for licensing from that entity. [FN105]

In response to these types of concerns, researchers have developed strategies to avoid these barriers. Academic scientists report regularly ignoring patents, and companies have rarely sought to prosecute them for infringement. [FN106] A recent ruling from the Federal Circuit has, however, made it clear that the experimental use exemption that many academics invoke does not protect them. [FN107] Infringement actions against universities, though rare, are not unprecedented, [FN108] and a few high-profile actions could quickly shift the tentative balance. [FN109] Moreover, there is still cause for concern if individuals are altering their research agendas or expending significant time and money trying to negotiate rights before deciding to infringe.

As we discuss in Part III, some universities have adopted the new strategy of negotiating formal research exemptions for themselves and other academic institutions. However, these exemptions may not extend to commercially-sponsored or -oriented research, limiting their efficacy. Outsourcing of research to jurisdictions where there are fewer patents [FN110] or ***1057** where robust research exemptions exist is another possible strategy, [FN111] but scientific research facilities and expertise will not always be mobile and transferring facilities abroad may entail significant costs.

Finally, neither formal nor informal research exemptions, nor outsourcing, will overcome the problem of blocking patents. [FN112] The right to research without the ability to commercialize an end product is of little value if we are concerned with improving worldwide health. Indeed, the anticipation of this problem may well be a more important research barrier than the costs and uncertainty associated with anticommons effects for public sector scientists.

D. Recent Proposals and Initiatives To Address the Access and R&D Gaps

The global access and R&D gaps have attracted substantial attention from scholars, [FN113] NGOs, [FN114] international bodies, [FN115] and various national ***1058** governments. [FN116] The increasing attention has generated a number of proposals and initiatives to ameliorate these problems. We focus on those proposals that address the static costs that patents can cause in developing countries, and that seek to stimulate R&D for neglected diseases, and/or target the problems of thickets and other barriers that patents pose to research. These solutions fall into two categories: top-down solutions, which require increased government funding and/or interventions in domestic or international legal regimes, and private sector action that relies on the voluntary initiative of firms.

1. Top-Down Change To Address the Access Gap

b) Proposals to reduce the difference between patent-based pricing and marginal cost pricing such as compulsory licensing schemes, [FN117] price controls, [FN118] changes to the TRIPS Agreement, [FN119] and alterations in national ***1059** patent laws in either rich [FN120] or poor countries [FN121] rely on concerted governmental action. Among these proposals, attempts to encourage developing countries to utilize the flexibilities available to them under international agreements has received the most sustained attention. The TRIPS Agreement, for example, affords member countries complete freedom to determine the grounds for compulsory licenses, [FN122] although it imposes restrictions on the process for granting them. [FN123] The recent Doha Declaration on TRIPS and Public Health has also given least-developed countries (LDCs) the right to refuse to offer product patents on pharmaceuticals until 2016. [FN124]

Unfortunately, such strategies are under attack. The United States is currently using free trade agreements to impose TRIPS-plus standards on dozens of countries around the world. [FN125] Several of these agreements limit compulsory

licensing to situations of emergency, public noncommercial use or to remedies for antitrust violations. [FN126] Almost all of the agreements ***1060** have data exclusivity provisions that may sharply limit or even eliminate the signatories' abilities to use the flexibilities provided in TRIPS and reaffirmed by the Doha Declaration. [FN127]

These trade agreements are subject to divergent interpretations, and countries could insist that the agreements be interpreted in ways that are consistent with the Doha Declaration. Furthermore, many countries have not yet signed such agreements and need only meet the minimum standards established by TRIPS. Nevertheless, the trend is clear. The most powerful governments on the international stage remain committed to an expansionist IP policy. In recent years, the United States initiated a dispute resolution aimed at Brazil's patent law, [FN128] threatened the South African government with trade sanctions because it sought to authorize the importation of cheaper medicines, [FN129] and repeatedly put countries such as Brazil, Thailand, India, and Argentina on the Special 301 watch list [FN130] because their patent laws did not meet with the approval of the U.S. pharmaceutical industry. [FN131] The access campaign has certainly drawn attention to this issue and achieved some victories in the short term. [FN132] However, both the United States and Europe have made it clear--through their positions in ***1061** bilateral and regional free trade negotiations and at the WTO [FN133]--that their policies are fundamentally unchanged and still aggressively favor strong IPRs.

The formal and informal pressures exerted by such nations circumscribes the willingness and ability of LMI country governments to use the flexibilities technically open to them. Until last year, Brazil was the only developing country that had successfully used the threat of compulsory licensing to obtain lower-price ARVs. [FN134] (Brazil, as one of the world's ten largest economies, [FN135] is in an unusually strong position for a developing country, and has substantial indigenous capacity to reverse engineer and produce medicines.) Only recently, and quietly, have other LMI countries began to issue compulsory licenses covering ARVs. [FN136]

Failures in accountability and leadership also contribute to the problem in some countries. Many governments are not committed to addressing the needs of the destitute sick within their borders. [FN137] For example, over the last decade, South Africa, India, and China have come under fire for denying the scope, or even existence, of the HIV/AIDS problem in their countries. [FN138] Finally, even LMI countries that have some will to address the access***1062** problem may be derailed by the inauspicious state of their intellectual property laws [FN139] and lack of expertise in applying these laws, as well as by the burdensome administrative conditions that TRIPS imposes. Because TRIPS requires a case-by-case determination of any compulsory license, developing country governments must establish administrative capacity to take consistent, rapid action wherever patents pose pricing barriers. [FN140] Similarly, TRIPS may create particular obstacles for countries without their own manufacturing capacity. [FN141] Some of these administrative costs can be lowered if countries gain experience using these channels. But given the likelihood that rich and poor countries alike will prioritize the wishes of corporate interest groups over the needs of the poor, no strategy involving top-down change alone is likely to remedy the static costs of the global IP regime.

2. Top-Down Change To Address the R&D Gap

Some of the most creative and promising proposals for addressing the R&D gap also follow a top-down model. Several academics have proposed prize systems to compete with or displace the patent system by rewarding inventors according to the therapeutic value their product ultimately***1063** offers. [FN142] Internationally, advocates have recently proposed an R&D treaty or convention that would set minimum levels of contribution to R&D and weigh national contributions to facilitate investment into neglected public goods. [FN143]

Most of the scholarly solutions proposed to address anticommons and thicket problems in the United States involve top-down change as well. For example, Richard Epstein has suggested that patent doctrine be interpreted to preclude the

patenting of genome fragments (known as expressed sequence tags or ESTs) that have more blocking value than use value. [FN144] The Federal Circuit's decision in Madey has spurred new interest in a statutory research exemption. [FN145] Professors Arti Rai and Rebecca Eisenberg have suggested that the Bayh-Dole Act, which allows recipients of federal funds to patent and exclusively license federally-funded research, [FN146] should be revised to give federal agencies more power to require ***1064** grantees to dedicate their research outputs to the public domain. [FN147] But, so far, all of these proposals have fallen on deaf ears.

The fact that the trend on the domestic and international stage has been towards stronger, rather than weaker, IPRs [FN148] bodes ill for the most ambitious of these top-down proposals. This suggests such strategies will need to be supplemented or catalyzed by solutions from another arena that can circumvent blockages within international and national political systems.

3. Private Sector Voluntary Concessions Regarding Access and R&D

Systemic change could also be initiated by the private, for-profit sector. [FN149] Unfortunately, history suggests that although the private sector can be pushed, it will not lead. Patent-based drug companies agreed to major price reductions for first-line AIDS therapies, but only after prolonged public outcry. [FN150] The experience of the Accelerating Access Initiative, a joint effort between U.N. agencies and five major pharmaceutical companies to achieve discounts for AIDS medicines for developing countries, is instructive here. A reporter for The Washington Post who interviewed most of those involved in creating the program has detailed its many failings and concluded that:

> ***1065** The drug firms sought to maintain prices in most markets by offering selective discounts that would remain under their control . . . [, i]n the long term, . . . building demand while limiting the duration and scope of the discounts. Most of all, the drug companies wanted to squelch an increasingly damaging debate on prices and patents that the U.N. agencies had helped touch off. [FN151] Even today, voluntary discounts have resulted in prices that typically remain above the lowest price for generic versions. [FN152] They are also often limited by territory or sector in ways that sharply undermine their impact. [FN153] In sum, they have been applied as grease to squeaky wheels--sporadically and no more liberally than is required to quiet the noise. As a result, voluntary discounts have proven neither efficient nor sufficient. [FN154]

***1066** The same holds true for voluntary licensing agreements. Until a few years ago, pharmaceutical companies routinely rebuffed requests for voluntary licenses on ARVs. [FN155] Following the Yale/BMS concession, several major firms offered licenses to South African generic companies, but limited them to the public sector. [FN156] Unfortunately, these licenses have remained few and far between. [FN157] Still today, MSF is unable to obtain voluntary licenses from patent-holding companies to use fixed-dose combinations of ARVs in South Africa and China. [FN158]

Additionally, while companies currently may look the other way when their AIDS drug patents are infringed in poor, heavily affected countries, [FN159] it is not clear that such forbearance will persist. It was not the ***1067** norm with regard to ARVs before the political tide turned, [FN160] and it will likely not extend to diseases that garner less political attention. Indications are that patent-based companies are still quite willing to use exclusive rights to extract rents in even the poorest countries. [FN161] Having advocated vigorously for maximum IP protections around the world, proprietary companies will presumably exploit the protections when they perceive it to be in their interests. It is fair to conclude, therefore, that the for-profit drug sector will not take positive action to address the static costs of IPRs in LMI countries unless others take the initiative and raise the costs of inaction for the for-profit drug sector. Furthermore, experience suggests that any such initiative must be carefully crafted to make commitments easy to enforce and to minimize withdrawal opportunities for companies.

There are only slightly more encouraging signs from the private sector in the R&D domain. Companies have done little on their own to develop drugs for neglected diseases, but some have been persuaded to contribute to the public-private partnerships we describe below. There are more promising signs that the private sector--or at least some parts of it--will help address the barriers that upstream patents can pose for researchers. Just as information technology companies are beginning to see the business sense in free and open source software, some companies that invest heavily in biomedical research are beginning to see the logic of investing in the public domain. Merck recently invested millions of dollars in a public genomics database because it "sees gene sequences as inputs, rather ***1068** than end products." [FN162] But, of course, companies that operate at the other end of the research spectrum have different incentives and are using their influence to prevent changes that would create more freedom for researchers. [FN163] Because firms have different interests in this area, and because it is unclear which side, if either, will prevail in a contest between them, we cannot rely entirely on the private sector to solve the problems that patents cause for research.

In conclusion, both theory and experience give us reason to believe that neither governments nor firms will act spontaneously and systemically to close the R&D gap, or to eliminate static costs created by the contemporary global IPR regime. [FN164] Given the stakes, there is an acute need for new models of IPR management.

III. MODELS AND LESSONS OF COMMONS-BASED PRODUCTION

In this Article, we propose two models that avoid roadblocks set up by governments and industry and that have the potential to catalyze wider change. These approaches draw on recent literature and experience with commons-based production modalities. We use the term "commons-based" to signify forms of production and coordination that rely on a mechanism other than proprietary exclusion and that treat all actors symmetrically vis-à-vis the resource in question. Commons-based initiatives offer a model by which a network of independent but interconnected participants can choose to act--not to change the legal system, but to change their practices within it. In so doing, they can circumvent barriers posed by standard applications of exclusive rights, such as patents and copyrights, and by rent-seeking lobbying that blocks statutory and regulatory change. These efforts do not rely on government action or private-sector, price-***1069** driven, market-mediated solutions, but on collaborative practices buttressed by contractual tools that apply property-like rights to ensure access and distribution rather than control and exclusion.

This Part describes the commons-based projects that have proliferated in recent years in the area of the production and distribution of information. It also discusses the innovative contractual forms that sustain many of these initiatives. Finally, this Part shows that universities and other public sector institutions are already beginning, in fragmentary and preliminary ways, to adapt some of these models to the biomedical domain.

A. Commons-Based Production Models

The wide range of open source and free software created by programmers who freely contribute their time and talent to collaborative efforts confounds the historic presumptions of property law. These presumptions say that property rights, price signals, and managers are necessary to organize and incentivize efficient production. [FN165] Free and open source projects, ranging in size from projects with merely two or three programmers to large-scale projects like the Linux kernel, use none of these presumptions and yet produce high-quality software that has come to occupy an increasingly prominent place in the information technology economy. [FN166]

Free and open source software could not have flourished in this way without the legal innovation embodied in the GNU General Public License (GPL). [FN167] The GPL was developed in the 1980s by Richard Stallman, a programmer

from MIT who sought a way to protect the historically collaborative mode of software development [FN168] from the encroachment of firms that wanted to make software proprietary. [FN169] The GPL has two key components. First, it gives users the right to copy, alter, and distribute the software source code, as modified or in its original form. Second, it includes a “copyleft” requirement, obliging those who create derivative code to grant the same rights to those who receive the derivative software. [FN170] Thus, the GPL not only shares but also requires others who benefit from the license to share their own contributions. The GPL turns copyright on its head, by guaranteeing rights to use, learn, freely distribute, and modify, ***1070** but not the right to exclude. This legal jiu-jitsu is well-suited to the cooperative nature of peer-produced software and its reliance on reciprocal sharing of innovation. [FN171] It has also been a model for other commons-based initiatives seeking to arm themselves against the rapid expansion of exclusive rights to information and culture over the past few decades.

Creative Commons is one of the most rapidly growing of these initiatives. It offers authors and artists a series of simple licenses that allow them to contract around the default in copyright law that reserves for them “all rights” in their creative works. [FN172] Using the Creative Commons website, individuals can choose between a menu of eleven licenses. The Attribution License, for example, permits content to be freely shared, modified, and commercially used, as long as the original author is given credit. [FN173] The Noncommercial License allows the same activities, but only for noncommercial purposes. [FN174] There is also a Share Alike license, which requires that any derivative works be distributed under the same terms as the original work. [FN175]

In the academy, commons-based production has become an important model for scientific publishing. The recently-created Public Library of Science (PLoS) offers peer-reviewed Internet-based content free to readers. [FN176] It covers the production costs of its journals with philanthropic donations and per-page-fees paid by authors and ensures the free distribution of articles by applying the Creative Commons Attribution License to them. [FN177] The National Institutes of Health (NIH) has recently adopted a policy intended to improve the public's access to publications resulting from NIH-funded research. [FN178] The policy calls upon scientists to submit the final-version-accepted-for-publication manuscripts to the NIH, and provides that the manuscripts will be made freely available on the Internet through the NIH's digital archive, PubMed Central, within twelve months of their final publication. [FN179]

***1071** Genomics research has been another major area for commons-based initiatives. The most prominent of such efforts is the Human Genome Project (HGP), a publicly funded, international research project that committed itself to releasing its data and not claiming patent rights in the mapped genome. [FN180] Many of the follow-on projects which seek to functionally specify genomic sequences and create maps useful for applied research have also adopted commons-based structures. The Ensembl Genome Browser uses open source software to create free, annotated maps of primarily mammalian genomes. [FN181] The HapMap project, which seeks to identify haplotypes (shared genetic variations) to help researchers better understand and address diseases with a genetic component, is also commons-based. [FN182] Like the HGP, HapMap makes its data available for free on the Web. Unlike the HGP, it took the additional step of creating a click-wrap license to prevent those accessing its data from combining it with their own data and patenting the results. [FN183]

The recently-launched Biological Innovation for Open Society (BIOS) project is perhaps the most self-conscious inheritor of both the lessons and tools of the free software movement. [FN184] A nonprofit created by the Australian organization CAMBIA, BIOS seeks to catalyze the creation of a new, ***1072** self-sustaining commons for researchers in the field of agricultural biotechnology. [FN185] It aims to do this by creating portfolios of essential biotech research tools and licensing them under a GPL-style license. The scientist behind the initiative, Richard Jefferson, has already created two technologies that engineer around proprietary tools critical for biotechnology-based crop improvement. [FN186] Licensees who want access to these technologies must accept the terms of the BIOS license, which requires them to share

and make available to other participants in the initiative any improvements they make to the core licensed technology. [FN187] Licensees are permitted to patent and license any products they develop--as distinguished from improvements on the tools licensed by BIOS--in whatever way they wish, and uses of the licensed technology are not limited by territory or field. BIOS, like the HGP and HapMap Projects, is betting that certain research tools are shareable, even in wealthy markets and under current IP regimes, because the tools' research value is greatest if they are freely accessible.

B. Lessons from Commons-Based Production Models

The initiatives described in the preceding Section represent a class of solutions to information production problems. They demonstrate that, in response to the new enclosure movement, collective action can successfully coordinate cooperative, open-access initiatives to produce and distribute innovations to target groups of users and researchers. The first lesson, then, is that commons-based modalities can play an important role in information production, including in the biomedical sector. The second lesson is that new contractual regimes are essential to the success of some of these initiatives. Only one of the projects mentioned above--the Human Genome Project--adhered to the classic public domain model and dedicated its outputs to the public without further restriction. Free software projects, the HapMap project (initially) and the BIOS initiative, all operate by conditioning access to their benefits on reciprocal sharing of appropriately defined improvements. They create a self-binding commons rather than an unrestricted public domain.

***1073** Because information is nonrivalrous, its sharing and use in a commons raises none of the allocation concerns characteristic of a physical commons. The only economic concerns raised by an information commons are ones of provisioning--that is, how the innovation will be paid for ex ante. [FN188] As we demonstrated in the preceding Part, where the information goods in question are specific to diseases affecting developing countries, innovation will likely have to be paid for by public or philanthropic sources because of the small size of associated markets. The right to produce drugs solely for use in LMI countries, or sharing rights to do research into diseases that disproportionately affect the poor, will therefore have little effect on incentives to invest more generally in commercial R&D.

It therefore comes as little surprise that biomedical research institutions, particularly in the public sector, are increasingly adopting commons-based strategies to promote production and access to information. Some have begun to utilize sharing principles to address the access gap, relying upon the fact that supra-marginal returns in developing countries are not necessary to the development of many health-related products. These initiatives piggyback on research funded by public or philanthropic institutions or by private investors seeking returns in rich country markets, and adopt contractual terms to ensure that resulting products will be available at low cost in developing countries. The Yale/BMS agreement not to enforce Yale's stavudine patent in South Africa is perhaps the most prominent example of this approach, but several others have recently emerged. For example, for technologies with a worldwide market, the NIH has begun to adopt licensing terms requiring North American and European companies to “provide a marketing plan for making products available to developing countries.” [FN189] The University of California at Berkeley recently signed a Memorandum of Understanding with the government of Samoa for rights to an antiviral compound, which the University hopes to develop into an AIDS drug. In the Memorandum, the parties agree that Berkeley will pay royalties to the government and local communities on sales of any eventual end product, and both parties agree “to license their respective intellectual property rights so that prostratin (if it is approved as ***1074** an anti HIV-AIDS therapy) is made available to developing nations at minimal cost.” [FN190]

Public sector institutions have also begun to adopt commons-based, open licensing approaches to address the R&D gap. In September 2004, the Office of Technology Transfer at the NIH announced its intention to develop U.S.-owned technology for a rotavirus vaccine by offering partially-exclusive, regional licenses to companies in developing coun-

tries. [FN191] This model suggests that by working with a diverse array of partners in LMI countries, innovators can find ways, even under current market conditions and without the injection of additional public or philanthropic funds, to develop technologies for neglected diseases and simultaneously minimize the costs to patients that result from exclusivity.

In recent years, a number of nonprofit initiatives have also been launched to address the R&D gap. Some of them seek to develop medicines or vaccines for global diseases that cause high morbidity in developing countries. Prominent examples include the Global Alliance for TB Drug Development (TB Alliance), the International AIDS Vaccine Initiative (IAVI), and the Medicines for Malaria Venture. Others focus on a broader range of diseases, such as the Institute for OneWorld Health and the Drugs for Neglected Diseases Initiative.

The exact mode of operation of each initiative differs, in part because of the different characteristics of the diseases they target, [FN192] but they generally***1075** support their operations through some combination of public and philanthropic funds and collaborations with private industry. [FN193] Those that have made their patenting and licensing policies public have indicated that they will either address access concerns by requiring their licensees to make subsequent inventions available, affordable, and accessible in target countries, [FN194] or by granting only nonexclusive licenses for sales to international agencies such as the WHO. [FN195] The TB Alliance also seeks to minimize patent barriers to research, and states that it will generally not seek patent protection on research tools "where the sole benefit of such protection is financial returns." [FN196] It also tries to ensure that licensees will continue to make technologies developed in partnership with the TB Alliance available to other entities conducting tuberculosis (TB) research. [FN197]

Universities have been active partners in such initiatives. In 2003, Yale University and the University of Washington granted OneWorld Health, a nonprofit drug company, an exclusive license to a novel class of high potency compounds, potentially effective against parasitic diseases common in the developing world. [FN198] The license allows OneWorld Health to develop the compounds for use against neglected diseases, while Yale and the University of Washington are free to pursue "a pharmaceutical partner to develop the same compounds for fungal infections in industrialized countries." [FN199] Early in 2004, the University of California at Santa Barbara donated to OneWorld Health "the patent rights to [a] class of cardiovascular***1076** medicines [for] their novel use as a potential treatment for schistosomiasis, a parasitic scourge that kills more than 200,000 people a year." [FN200]

Universities have also become more proactive about reserving rights in licensed technologies for their own research purposes and sometimes also for other academic institutions. [FN201] The NIH has strongly encouraged them in this direction. [FN202] The most common approach appears to be to reserve rights only for the licensed technology or materials, and only for noncommercial research. [FN203] However, two more ambitious examples exist. Stanford University's model exclusive licensing agreement reserves rights for commercial as well as noncommercial research for both itself and other universities. [FN204] The Wisconsin Alumni Research Foundation (WARF), the holder of the University of Wisconsin's stem cell patents, reserves rights only for noncommercial research, but it captures improvements into the scheme and also retains the right to sublicense to governmental agencies and nonprofit research institutions. [FN205]

Such individualized initiatives are limited and must each bear the cost of negotiating around barriers to research on their own. Collaborative responses hold more promise because they can pool resources and further ***1077** reduce transaction costs. The recently-created Public Intellectual Property Resource for Agriculture (PIPRA) illustrates the promise of this approach. [FN206] Faced with substantial fragmentation as well as exclusive public-to-private licensing of IP rights, several public sector agricultural research institutions founded PIPRA to improve management of IP resources. [FN207] PIPRA's members include more than twenty major academic research institutions who have committed themselves to collaboratively facilitate the development and dissemination of crops for developing countries. These institutions are exploring several possible approaches, including a standard research exemption that would preserve their rights to issue li-

censes for research and distribution of products in developing countries, [FN208] and a public-sector database that would assist scientists in obtaining information about patent landscapes. [FN209]

These initiatives are first steps along the path of commons-based production, and as such, many of them only partly protect the interests of patients and researchers. But they show that public sector institutions are willing to explore such initiatives, even though the institutions have yet to agree on a strategy that maximizes their collective potential. Public sector institutions--universities chief among them--can implement the solutions outlined here, if these implementations are informed by a careful assessment of the barriers that IPRs can pose for access to medicines and research. The remainder of this Article applies these lessons to create a collective, standardized strategy that universities and other public sector institutions can adopt to govern innovations that have public health applications in LMI countries.

***1078** IV. THE CASE FOR UNIVERSITY ACTION

Although universities played a significant role in the various commons-based initiatives discussed in Part III, they have yet to consolidate their efforts in the biomedical domain. This may be poised to change. First, universities play an important role in the biomedical R&D system in the United States. This gives them the power to act to improve the lives of patients and also to collectively persuade private sector partners of the need for an open licensing approach. Second, key members of university communities, from researchers dedicated to open science to students and faculty committed to social justice, will likely support and even demand such a change. Third, there is no significant economic risk associated with the shift--to the contrary, it has the potential to increase the resources available to universities.

A. The Role of Universities in Biomedical Research

Universities are responsible for more than half of the basic research in the United States. [FN210] Their relative importance to the R&D system is significant and growing: they conducted 14.5% of all R&D activity (both basic and applied) in 1997, nearly double the proportion they conducted in 1960. [FN211] The majority of all academic research is still funded by the federal government, [FN212] and although the importance of private sector funding is growing, it does not provide even as much financial support as academic institutions themselves. [FN213]

Although universities specialize in basic, upstream research intended to advance scientific understanding and to develop the tools of the research field, [FN214] "it is a fallacy to think of U.S. university research as traditionally***1079** 'basic' and conducted with no attention to practical objectives." [FN215] In fact, university researchers frequently create new advances in areas as diverse as medical devices, computer software, and scientific instrumentation. [FN216]

A host of economic studies have confirmed that public sector research, including research done at universities, is a central contributor to R&D in some industries, and particularly in pharmaceuticals. [FN217] In a survey published in 1991, companies in the drug industry reported that seventeen percent of their products and eight percent of their processes were very substantially influenced by academic research, and that in the absence of academic research, twenty-seven percent of their new products and twenty-nine percent of new processes would have been substantially delayed. [FN218] Similar results have been confirmed by other studies. [FN219]

Universities have long engaged in commercialization and patenting, but the scope and nature of these activities has changed profoundly over ***1080** the last twenty-five years. [FN220] The number of U.S. patents granted annually to U.S. academic institutions grew more than ten-fold between 1970 and 2001. [FN221] In fact, from 1993 to 2003, the number of patents issued to respondents of a survey of leading research universities more than doubled. [FN222] Licenses have

increased concomitantly: American universities, hospitals, and other nonprofit research centers concluded more than 4,500 license and option agreements in 2003, more than double the license and option agreements executed in 1993. [FN223] A major share of these university patents are in the biomedical field. [FN224]

Accompanying this growth in patenting and licensing, the number of university technology transfer offices (TTOs) has increased dramatically. [FN225] TTOs identify, protect, market, and license university IP for ***1081** commercial use. Thus, TTOs are the key institutional player in universities' increasingly focused and proactive approach to securing IPRs. [FN226]

Turning to current practices, universities frequently patent the research tools they develop, and have been criticized for licensing some very important tools exclusively. [FN227] Universities have also come under fire for what many perceive as overly aggressive terms in research tools licenses. Typically, when licensing to private firms, universities seek fees or reach-through royalties on resulting products. [FN228] Furthermore, "[e]ven when they do not seek patents, universities often seek to preserve their expectations for profitable payoffs by imposing restrictions on the dissemination of research materials and reagents that might generate commercial value in subsequent research." [FN229] A review conducted by the NIH concluded that universities have sought just about every kind of clause in research tool licenses to which they themselves have objected, including publication restrictions, rights in or the option to license future discoveries, and prohibition on transfer to other institutions or scientists. [FN230] As noted above, it appears that universities are beginning to reserve research rights for themselves and other academic institutions when they issue exclusive licenses, but the reach of these clauses is often limited to noncommercial research. [FN231]

Where an invention has potential to be developed into a pharmaceutical product, universities will typically patent it in the United States, ***1082** Europe, Canada, Australia, and Japan. [FN232] There is no comprehensive data on the overall ownership position of universities in current pharmaceutical technologies, but the aforementioned trends in R&D and patenting suggest their ownership share is both substantial and increasing. In recent years universities have obtained U.S. patent rights in a number of key pharmaceutical products, including: the cancer drugs cisplatin and carboplatin, [FN233] pemetrexed (Alimta), [FN234] and cetuximab (Erbitux); [FN235] the anemia treatment epoetin alfa (Epogen); [FN236] the AIDS drugs stavudine (Zerit), [FN237] 3TC (Epivir), [FN238] abacavir (Ziagen), [FN239] and T20 (Fuzeon); [FN240] and the best-selling glaucoma medicine latanoprost (Xalatan). [FN241] Universities also hold patents on essential manufacturing processes. [FN242]

A TTO will also decide in which foreign countries it wishes to patent. [FN243] This decision appears to be based on a narrow economic calculation,***1083** measuring the expected net present value of exclusivity against the cost of obtaining and defending a patent, and without factoring in non-economic considerations, such as access to medicines for LMI country residents. [FN244] While there is no comprehensive data and no easy way to determine patent status in the majority of LMI countries, [FN245] universities report that few of their inventions are patented in LMI countries because the benefits of exclusivity rarely justify the cost of securing patents. [FN246] However, the more likely a technology is to have application in a developing country, the more likely it is the economics will weigh in favor of patenting. The calculus shifts further in favor of patenting if a private sector licensee is willing to bear the associated costs. In that case, universities typically permit licensees to decide where to patent-- although most universities retain the patents in their own name. [FN247]

If the innovation is intended as a pharmaceutical or diagnostic end product, it will typically be licensed under a worldwide exclusive license, [FN248] often to a small start-up company, [FN249] which will usually develop the product further before sublicensing it to larger firms. [FN250] In exchange for exclusivity, the university will typically receive royalty payments ***1084** and/or equity in the licensee. [FN251] Due diligence clauses are also commonplace, to ensure

that the university technology does not lay fallow. These clauses oblige the licensee to develop the compound--to conduct clinical trials and other developments necessary to market the product--or face revocation of the license. [FN252]

Because universities license their technologies in order to secure the investment and expertise necessary to further develop and market the technologies, the university's licensed patent will frequently be a key component, but not the entirety, of the rights necessary to generate the end product. The licensee may acquire secondary or improvement patents on subsequent developments such as dosages or delivery systems. [FN253] The licensee will also generate the safety and efficacy data needed to market the drug, and will be able to exercise exclusive rights over this data. [FN254]

B. Institutional Principles and the Internal Political Economy of Universities

1. Open Science and the Goals of Technology Transfer

Universities' core institutional principles include the production and dissemination of knowledge, as well as a related and more general dedication***1085** to improving human welfare. The centuries-old academic tradition of open scientific practice [FN255] faces increasing pressure from universities' patenting and commercialization activities. As a result, these policies, and the TTOs that administer them, have come under attack. [FN256] Because a TTO's performance is generally measured by licensing revenue, [FN257] TTO professionals have incentives to aggressively seek patents and high licensing fees, which the research community as a whole might rather forego. [FN258]

There is, however, nothing inherent in the existence of university patents or of TTOs that requires that this be the case. TTO incentives would change if contributions to health, particularly global health, were made a part of the calculus. As access concerns have come to the forefront, leading members of the technology transfer community have shown signs of supporting steps to address health concerns of the developing world. [FN259] Universities, after all, are different kinds of organizations than pharmaceutical firms: they have different revenue structures, different R&D investment***1086** motivations, and different cultural self-perceptions. [FN260] To the extent universities have managed their patent portfolios as though the universities were for-profit firms, it is a result of a failure to properly define the universities' interests and power as holders of significant patent stakes. A narrow focus on maximizing the amount of revenue generated by university discoveries is difficult to reconcile with the spirit of university patent and licensing policies, which typically declare that the ultimate purpose of technology includes the advancement of the public good. [FN261]

As Yale's experience with stavudine demonstrates, the conflict between a university's ethos and its patenting practices can erupt into public protests from both students and faculty: students organized to support MSF's request for a patent concession, and one of the scientists who had discovered that stavudine could be used to treat HIV voiced his disapproval of the university's practices in the New York Times. [FN262] A student-led group, Universities Allied for Essential Medicines (UAEM) continues to challenge closed licensing practices at universities, [FN263] while the academic community is giving increased attention to the access and R&D gaps. The campaign for divestiture from South Africa, and the more recent anti-sweatshop movement targeted at university apparel, [FN264] demonstrate that student-driven protests can produce changes in university policy. For institutions dependent on philanthropy and government funding, the goodwill gained by acting to alleviate the access gap is potentially significant,***1087** while the negative publicity from exposure of internal fissures over this issue may be damaging. In addition, to the extent the behavior of their TTOs deviates from the public interest, universities may face other, potentially less-expected risks. [FN265]

Finally, it is worth noting that the NIH will unlikely step in to resolve these tensions. Although the Bayh-Dole Act gives the agency the authority to “march in” on patents to ensure that federally-funded inventions are accessible to the public, [FN266] the NIH has so far rejected every request that it use these powers to make medicines more accessible.

[FN267] The NIH also "has no authority under the Bayh-Dole Act to issue broadly applicable substantive regulations concerning the licensing of inventions (as distinguished from making specific determinations regarding march-in rights in the context of particular grants)." [FN268] This substantially limits the NIH's ability to deal with barriers caused by patents on federally-funded research ***1088** tools. [FN269] In other words, if change in university practice is to occur, it will likely have to be initiated by universities themselves.

2. The Economics of Technology Transfer and the Access Gap

Fortunately, adopting the proposals made in this Article is financially viable for universities. To begin, universities do not rely substantially on technology transfer revenues. Although TTOs have managed to obtain tens of thousands of patents, they tend to remain money-losing endeavors. [FN270] The number of schools that make money from technology transfer is small, and those that profit tend to do so from a limited number of highly successful patents. [FN271] Licensing revenues are typically equivalent to just four percent of a university's research funds, and this figure decreases significantly when the costs of patent and license management, as well as the inventors' share of royalty income, are subtracted. [FN272] When patent royalties are compared to total university revenue, they appear quite small, constituting only 0.5 to 2% of revenues, even for the subset of universities that are patent-productive. [FN273]

Most significantly for our purposes, the proportion of revenue that a university would obtain from developing countries, even on a blockbuster drug, will be vanishingly small--only a few percent of those few percent of total revenues that PhRMA companies make in LMI countries. [FN274] Yale reported no lost revenue as a result of the stavudine patent concession in ***1089** South Africa, and Yale's Dean of Public Health Michael Merson stated that "[t]his change was made at Yale without any negative consequences to the University--financial or otherwise." [FN275] Universities could even financially benefit from adopting the policies we propose, if at the margins it helped them to attract scientists, students, or funding for research.

Because of the small size of the LMI market, patent-based pharmaceutical firms can promote access at minimal cost, and without sacrificing profits to any substantial degree, simply by allowing generics to enter LMI markets. The same is true of efforts to free up research on neglected diseases or developing country indications for existing medicines; because such companies do not currently seek revenues from such research, allowing others to do it will not affect their profits.

The pharmaceutical industry's increasing dependence on external research, including university research, to fill its R&D pipelines and provide it with research tools [FN276] further suggests that universities can promote research and access without material risk of losing deals, reducing income, or jeopardizing the viability of technology transfer operations. This is particularly true if universities act collectively and in a standardized fashion rather than trying to promote access on a deal-by-deal basis. While pharmaceutical and biotechnology companies will likely resist any changes to the status quo, if major research institutions act together to implement new practices--and thereby redefine the norms--pharmaceutical and biotechnology***1090** companies will have little choice. While an individual university may be dispensable to the pharmaceutical industry, universities in aggregate are not. [FN277]

V. WHAT UNIVERSITIES CAN DO

If universities are to harness the potential of their technologies to close the access and R&D gaps, they must formulate a strategy that will help them achieve these goals. This strategy must be easy to use, to allow even those universities with the fewest resources to implement it. It must also be highly standardized, to capitalize on universities' collective influence and bargaining power. Below, we elaborate two commons-based approaches that meet these criteria and are configured to serve the needs of people living in developing countries.

A. Addressing the Access Gap: Equitable Access Licensing

Part II demonstrated that the price differential between exclusivity-based pricing and marginal-cost pricing can constitute a serious barrier to access to medicines for people living in the developing world. Here we describe an approach called Equitable Access ("EA") licensing as a means of removing that differential. This mode of licensing, like the licensing practices that govern free software, uses proprietary rights to secure freedom for an open class of potential users, rather than to secure exclusivity for a closed class of licensees. Like the GPL, it uses IPRs not to exclude and monopolize, but rather to ensure the right of third parties to access and distribute the innovation and its derivative products. Finally, the EA license is commons-based because it seeks to use the university's rights to create a self-binding commons--a universe of information resources necessary to produce the end product--that is open for all to use. This freedom,***1091** we predict, will entice other actors to provide the end product at a competitive price.

Simply stated, an Equitable Access License is one that seeks: (1) to ensure freedom to operate for any party that manufactures and distributes the licensed technology and any derivative products in LMI countries, and (2) to minimize administrative overhead and political contingency by initiating a self-enforcing open licensing regime.

1. The Choice and Definition of the "Freedom To Operate" Approach

Theoretically, if a university developed a drug, vaccine, or diagnostic tool from its lab bench to the pharmacy shelf without any partners, it could eliminate supra-marginal cost pricing in developing countries by simply not patenting or seeking other exclusive rights in these territories, and allowing anyone to export the university's development. [FN278] However, this is not generally how R&D happens. Universities operate in a universe where they are not the only holders of IPRs, and they frequently contribute only at one stage in the value chain. Non-patenting alone will not, therefore, ensure that generics will be available in LMI countries, just as releasing copyrighted works into the public domain will not ensure that derivative works will remain open for anyone to use, modify, and distribute. To resolve this problem, EA clauses must adopt the strategy used by the GPL--they must leverage the exclusive rights associated with a patent to ensure accessibility of derivative products.

An initial choice faces any innovator who wishes to do this: whether to adopt a fair pricing approach or implement a freedom to operate strategy. Under the first option, the licensor would oblige its licensee to distribute the end product in the selected territories quickly, in sufficient quantities, and at the marginal cost of manufacture. Under the second option, what we call the "freedom to operate" approach, the innovator uses open licensing to achieve the goal of marginal cost pricing. Ensuring freedom to operate here means guaranteeing third parties the right to compete in a market without being blocked by patents or other forms of exclusive rights. It does not mean guaranteeing third parties the active transfer of materials or know-how to assist their production of a generic alternative--or what we term "enablement." The choice between these options is essentially a choice between heightened regulation of the licensee's behavior and contractual deregulation of the end-product market.

***1092** The fair pricing approach might appear, at first blush, to be the most direct and efficient means of achieving marginal cost pricing. After all, the licensee need not incur the cost of reverse engineering, will have existing production capacity, and may also be able to take advantage of economies of scale. Some licensees may also prefer this option, as it offers them more control than does the freedom to operate approach. But a strategy that relies on freedom to operate will generally produce better results for both patients in LMI countries and for universities, for several reasons.

To begin, the freedom to operate approach is preferable for universities because it does not require them to take an active role in monitoring or enforcement. This approach avoids placing any ongoing demands on universities or their licensees by introducing a third set of players--typically generic companies--with market incentives to narrow the access

gap by offering low-priced, but still profitable, products. A university that signs a fair pricing clause, on the other hand, must be willing to monitor the clause's implementation and make a credible threat to bring legal action against a defaulting licensee, or to deem the licensee in breach and revoke the overall license itself.

In principle, the empirical challenges of the monitoring role can be overcome. [FN279] But monitoring all of these issues would require universities to devote substantial resources to the task, and enforcement would constitute an even more costly endeavor. [FN280] Universities are not all equally able to invest in monitoring or enforcement of licenses, and even the best-situated universities will have limited resources to devote to such activities. Moreover, the fact that universities are repeat players in a game ***1093** where reputations often travel quickly is likely to discourage aggressive monitoring and enforcement. [FN281]

Second, the freedom to operate approach can be expected to provide patients in LMI countries with cheaper medicines than the fair pricing approach would. Experience indicates that generic companies will almost always be able to undercut the “at cost” prices of proprietary firms. It is not clear whether proprietary products have higher marginal costs, whether companies calculate marginal cost in different ways, or whether proprietary companies are simply being dishonest when they claim to be selling at cost. Regardless of the reason, it is clear from available evidence that competition has been more reliable as a method of lowering prices than voluntary “at cost” pricing. Again, because patients and even governments in LMI countries are extremely sensitive to even small differentials in price, the freedom to operate approach has a substantial advantage here.

The prevailing legal environment gives the freedom to operate model a third advantage over the fair pricing strategy: it can reduce the risk of both physical and price arbitrage. Differentially priced products sold by the originator company may be susceptible to parallel trade. [FN282] The freedom to operate approach sidesteps this issue by relying upon generic provisioning to reach marginal cost pricing. Due to patent barriers, generic versions are not susceptible to parallel trade in the same way as originator products may be. Licensees may also express concerns about the generic products illegally finding their way into high-income countries. There is no empirical evidence of any substantial flows of medicines from LMI to rich countries; [FN283] but insofar as this is a concern, an EA clause can address it in the ***1094** same manner that the WTO has treated the issue--by requiring use of different packaging, pill color, and pill shape to facilitate identification of illegal importations where this is feasible and does not significantly increase the price of the product. [FN284] In theory, generic provisioning also ought to assuage some of the licensee's concerns--whether justified or not--about what we might call “politically mediated arbitrage,” where discounted prices in one country fuel public demand for lower prices in another. [FN285]

Finally, the freedom to operate approach is preferable because it will tend to generate a more sustainable and appropriate supply of low cost medications in LMI countries. This approach puts a thumb on the scale of technology transfer by presenting a small--but, for generic companies, meaningful--market to attract the investment necessary to reverse engineer and scale-up production. The long-term health of the generics industry requires a diffusion of technical knowledge and markets sufficient to sustain what is widely acknowledged to be a very low margin business. Encouraging competitive provisioning in LMI countries will foster and sustain the development of diverse nodes of technological capability necessary to reverse engineer and manufacture medicines.

2. Transactional Flow

In order to achieve freedom to operate and to minimize administrative overhead, we propose adapting commons-based approaches to create a self-enforcing open licensing regime for biomedical R&D. Under this approach, when a university licenses a health-related technology to a firm, the university obtains all of the necessary rights to ensure freedom

to operate in LMI countries for any resulting products. This requires that any rights in an end product which belong to the licensee must be transferred to the university via a grant-back and cross-licensing structure. [FN286] The ***1095** transferred rights only allow the university to grant licenses to third parties who wish to supply the end product in LMI countries. To take advantage of these licensing terms, the third party licensee must simply notify the university and the university's licensee of its intent to operate under the protection of the EA clause.

a) Identifying Appropriate Technologies and Beneficiaries

i) Target Technologies

The first step of EA licensing is to identify an appropriate technology. Generally speaking, EA licenses will be most appropriate and feasible where the value of a technology is clear and the university controls a good deal of it. The EA approach will be more difficult to apply to technologies that are inchoate or where technologies clearly have small potential commercial value. Much depends, in other words, on a university's bargaining power--which, as noted above, can be substantially increased if universities adopt a standardized, collective approach.

Because the EA approach seeks to share aspects of an innovation that have little commercial value, it should be possible to use the approach when licensing a wide variety of technologies. The most obvious candidates are potential pharmaceutical products, both “small molecule” drugs (for example, aspirin, cisplatin, and stavudine) and “biologic” therapies (for example, insulin, Epogen, and Herceptin). [FN287] Small molecule compounds are readily reverse engineered, and thus are ideal candidates for EA licensing. Biologics--which include a wide array of therapeutic protein products, from vaccines to monoclonal antibodies--present a potentially more complicated situation. This is due to the increased complexity associated with the production of biologics. [FN288] While there is no reason to ***1096** categorically exclude biologics from EA licenses, ensuring freedom to operate in this context may require additional steps.

Although often neglected in discussions focused around access to medicines, diagnostic technologies--for example, those that may help more accurately diagnose cervical cancer or determine whether people with HIV have tuberculosis--should not be ignored. They are essential to the doctor's arsenal, and may be highly amenable to an EA approach.

There is no reason why universities could not also assert EA requirements when licensing manufacturing technologies or even upstream research tools like gene targets. In the past, some universities have attempted to obtain reach-through royalties on upstream innovations such as cell lines or drug screening tools. [FN289] It should therefore be possible for universities to seek access provisions with a similar reach-through structure.

***1097** Finally, a technology appropriate for EA licensing ought to be health-related. [FN290] As long as this standard is met, an EA clause should be applied, regardless of the type of health condition the product addresses. Universities should resist the pervasive tendency to presume that access concerns in developing countries are limited to drugs for diseases such as HIV/AIDS, TB, and malaria. This tendency is encouraged by pharmaceutical companies, and fuelled by the dangerous misconception that chronic, noncommunicable diseases do not affect developing countries, only affect the elderly, or cannot be effectively treated and prevented. [FN291]

The majority of the global burden of chronic, noncommunicable diseases such as diabetes, cancer, cardiovascular disease, and chronic respiratory disease-- life-threatening conditions for which a significant and growing array of medicines is available in high-income countries--is borne by those living in developing countries. [FN292] As their prevalence increases, such diseases become an even more pressing public health concern. [FN293] Cardiovascular diseases, malignant neoplasms, and chronic respiratory diseases each cause more deaths in developing countries than does HIV/AIDS. [FN294] These conditions are not only common in developing countries, their implications are also more severe. Indi-

viduals in developing countries tend to die sooner and at a higher rate from chronic diseases than do individuals in ***1098** high-income countries. [FN295] Although the treatment of communicable diseases generates a distinct set of positive externalities, [FN296] from both a health and human standpoint, there is no reason to distinguish between types of diseases or medicines.

Universities should therefore apply EA licensing to technologies relevant to all diseases, including medications for cancer and heart disease, interventions related to diabetes, and so forth. Indeed, EA licensing may be more effective to alleviate the disease burden of “global diseases” like cancer and diabetes than it will be for neglected diseases. Where a university technology only has an application in developing countries, the innovation is unlikely to be developed without a partner, such as the Drugs for Neglected Diseases Initiative. Such partners will themselves be both motivated and well-suited to address access concerns, meaning that it may either be unnecessary or superfluous to insert EA terms into these licenses.

ii) Identifying Beneficiary Countries and Sectors

An EA license must also identify beneficiary countries and beneficiary sectors within these countries. We contend that, in order to meet the health needs of patients in developing countries, EA provisions must include middle-income countries, as well as the right to supply the private sector in LMI countries. Excluding these markets would substantially undermine the university's attempt to address the access gap.

It is true that some middle-income countries have rapidly growing economies, and may come to represent a larger percentage of the pharmaceutical market over the years. Of course, those that grow sufficiently to be recognized as high-income countries will no longer be beneficiaries of the license. In the meantime, middle-income countries are characterized by highly unequal income distributions. [FN297] Although some residents in ***1099** middle-income countries are wealthy, a large portion of them are destitute. [FN298] And, they, along with the poor in low-income countries, typically must obtain their own care in the private sector. [FN299] If EA licenses limit low-cost generics to the public sector in LMI countries, or exclusively to low-income countries, they will leave out many individuals who universities aim to benefit. [FN300]

Additionally, excluding middle-income countries threatens the potential effect of EA provisions in the place they might otherwise work best. EA provisions are most likely to be applied to medicines that will be developed for wealthy country markets, such as those addressing chronic, noncommunicable diseases. As between low-income and middle-income countries, it is in fact middle-income countries that are in more acute need of such medicines. [FN301]

Moreover, both middle-income countries and the private sector generally are critical to ensure that there are sufficient incentives to sustain the generic companies providing the medicines in question. As profit-seeking enterprises, they must evaluate whether the available markets justify their investment in reverse engineering and scaling-up production; these relatively larger markets figure prominently in this determination.

Finally, any line dividing markets within or between nations is in some sense arbitrary. In theory, some combination of measures that would more finely track income, disease prevalence and distribution, and the purchasing power of the public system would likely be more satisfying intellectually***1100** than a simple geographic/income based division. Universities could try to set up a process to evaluate the effect upon patients of excluding particular middle-income countries or the private sector in select LMI countries, but we suspect that this would not be worth the effort. Because profits from such countries and sectors are unnecessary to stimulate product development, and given the extreme difficulty of defining and implementing distinctions that are more closely tailored to poor patients' ability to pay, the optimal distinction will likely be the one drawn between high-income countries and LMI countries.

b) Flow of Rights

EA licensing involves limited cross-licensing between the university and its licensees, structured to create freedom to operate for third parties for the benefit of LMI country distribution. [FN302] In exchange for permission to use the university's exclusive rights in high-income countries, the licensee and its sublicensees cross-license exclusive rights they own in the end product to the university. This cross-license is limited and available only for the purpose of an automatic sublicense flowing from the university to any third party who notifies the university and licensee of its intent to supply an LMI market and fulfills some additional requirements (we refer to this third party as “the notifier,” or, where relevant, as “the improver”). The university need not hold a patent in the LMI countries where the drug is to be distributed. It is only necessary that the university own technology that the licensee wishes to use, in exchange for which the licensee agrees to the limited cross-license. After the initial agreement is reached, to obtain freedom to operate, all the generic manufacturer need do is notify the university and its licensee. It thereby receives a limited license to all of the patents that belong to the university or its licensees that are necessary to produce the ultimate end product for distribution solely in LMI countries.

i) Cross-License and Grant Back

The first transactional element of an EA license is an exchange of licenses. The university grants to the licensee rights to a particular technology or innovation, and sets the parameters of the license. The license will likely include, at a minimum, rights to practice the university's technology in some or all high-income countries. In exchange, the licensee will cross-license to the university its “associated rights.” These rights must include ***1101** all of the potentially exclusive rights it holds that could prevent a third party from producing or delivering an eventual end product, including rights in any patents and data possessed by the licensee during the term of the license that are necessary to make, use, sell, import, or export the end product. This right does not reach know-how or any other secret or material property possessed by the licensee. It would, however, cover associated rights that the licensee possessed or developed that do not rely directly upon the university technology but are nonetheless necessary to the production or sale of the end product.

In coming years, rights to clinical trial data are likely to become an increasingly important tool of exclusion in developing countries. [FN303] EA clauses must therefore include such data in the bundle of rights received from the licensee and openly sublicensed to the notifier. Within the EA model, the license to use data means only that no exclusive rights will prevent the generic company from relying in its application on publicly available data generated by the licensee or the fact that the drug has been registered in another country. [FN304] The license removes the formal right to exclusivity. It does not give a notifier the authority to obtain otherwise nonpublic data from the university's original licensee. The generic producer will, of course, still have to meet other regulatory requirements related to bioequivalence and manufacturing standards, to the extent these requirements exist in the notified country.

The university obtains these rights for the sole purposes of providing freedom to operate in LMI countries. Although in some circumstances grant-back arrangements for open source projects may implicate the patent misuse doctrine, [FN305] this does not appear to be a concern in this case. [FN306] Figure 1 illustrates this initial transactional flow.

***1102** Figure 1: EAL Transaction Flow Phase 1

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ii) Notification

The second transactional component of an EA license is an automatic open licensing structure organized around a

simple notification procedure. This component's core attribute places power to act in the hands of a third party, typically a generic company. Any disputes about the applicability of the freedom to operate are left to the licensee and the party seeking to enter the market, permitting the university to remain largely out of the picture. Figure 2 illustrates this transaction.

***1103** Figure 2: EAL Transaction Flow Phase 2

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EA provisions are triggered when a third party notifies the university and licensee that it intends to make, use, or sell the end product in, or import the end product into, an LMI market. The notifier can be any entity, but we anticipate three primary users of the notification procedure: (1) generic companies that wish to produce or sell in an LMI country; (2) a government agency such as a ministry of health, or NGO such as MSF, that wishes to import generics from a third party; or (3) a researcher who wishes to adapt the end product for developing country use.

In order to foster a competitive environment, the EA model presumes that multiple entities may notify for a particular market. Although it would be possible to arbitrarily limit the number of firms that could notify, and thereby shelter the first notifiers from a fully competitive environment, this has obvious risks. Over time some form of limited exclusivity might be required to induce generics to introduce a product to market. But at this time, there is no clear evidence of this need, and generic manufacturers have entered LMI markets when patents did not present a barrier without promise of exclusivity. Should practice indicate that some stronger inducement is necessary, the standard approach could be revised to offer a limited period of exclusivity for the first notifier that brings a product to market in a particular country. [FN307]

***1104** Upon notification, the open licensing provisions of the EA license are engaged. The university's licensed rights, including associated rights from its licensee, flow to the notifier for the sole purpose of manufacturing for distribution and distributing in the notified country. Patent, regulatory, and manufacturing barriers are lifted for the notifying entity by this flow of rights. This can be achieved by a statement in the EA license that a notifier shall receive from the university an open license permitting the making, using, selling, offering to sell, importing, and exporting of the end product in the notified country. A royalty payment could be required in consideration for the open licenses. For low-income countries, the license could specify a rate within the range recommended by UNDP of zero to six percent. [FN308] Because middle-income countries can afford more, on average, sales in these countries could be subject to a slightly higher flat rate. [FN309] Finally, the license will also have to establish an equitable division of royalties between the university and the licensee.

It is important to note that this model permits production of the end product in any country (including a high-income country), as long as manufacture is for the sole purpose of exporting to and supplying the end products in the notified country. This will increase the likelihood of finding a generic supplier for more complicated drugs. It will also create maximal competition in the market to supply LMI countries, which in turn will drive prices towards marginal cost.

***1105** iii) Notifier Improvements

If the EA license defines the terms “end product” and “open license” appropriately, it can also operate to permit notifiers in any country to engage in research to improve the end product. This could substantially benefit patients because it would allow companies and academic researchers in those countries to adapt the technology to local circumstances in a way that a proprietary company might be unwilling or unable to do. For example, the first three-in-one pill for AIDS patients was developed not in the United States or Europe, but in India--and it was created without any guarantee of exclusivity. [FN310] As described in Part II, many products must be altered in specific ways to meet the needs of patients in

developing countries. Some of these modifications, such as pediatric dosing, require minimal investment and are currently being undertaken by generic companies. [FN311] These examples suggest that if potential innovators are ensured freedom to experiment and sell improved versions of products in LMI countries, we may see not only cheaper products in these countries, but better ones as well.

To meet these goals, however, any such improvements should be licensed back to the university for the sole purpose of sublicensing them under EA terms to subsequent notifiers in LMI countries. The notifier's improvements would themselves be subject to the EA terms. The notifier would be paid royalties for the use of its improvements in LMI country markets, but the notifiers could not prevent others from exploiting the improvements.

Some might advocate allowing the improver to patent its own improvements in high-income countries and then to negotiate the necessary cross-licenses with the university and/or licensee. The opportunity for a potentially lucrative cross-license might offer the notifier an incentive to make innovative improvements (although it is not immediately clear how well these would align with the improvement needs of LMI markets). The alternative is to include in the EA license a requirement that the improver grant the university and/or licensee an option to license any improvement. The EA license could specify the terms of this option, namely a reasonable royalty rate for licensing the improvement.

***1106** We have now described the complete flow of rights associated with an EA license. Figure 3 illustrates this transactional flow.

Figure 3: EAL Transaction Flow Phase 3

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iv) Resolving Disputes

Under an EA license a notifier is automatically deemed to have an open license; therefore, it may immediately and lawfully begin to sell the end product in the specified LMI country without infringing upon any rights held by the licensee or sublicensee. [FN312] An EA license is itself the legal protection provided to any entity making use of the license's provisions. While structured as a license, it operates at a minimum as a covenant by the university and its licensee not to sue entities that rely on technology to which they have rights solely for the EA license purposes. There is some legal risk involved for the entities that seek to rely on the EA license, because of the potential for variations between jurisdictions with regard to such third-party reliance on the provisions of a license to which they were not a party. Nonetheless, because of the relatively widespread use of covenants not to sue and the small value of the markets covered, that risk is likely to be manageable. Generics always have the option of ***1107** also seeking a more direct license. If they do so, the existence of the threat to operate under the EA license as a fallback is likely to improve the entrants' negotiating position. [FN313]

If the licensee or the university wishes to contest the applicability of the license to the product or patents included in the notification, they may of course do so, by challenging the actions of the notifying party and/or taking legal action. A notifying party operating inconsistently with the terms of the EA provisions (for example, by seeking to sell in a high-income country or seeking to sell products that are not covered by the license) will infringe the underlying patent rights and will be subject to the usual remedies for patent infringement.

v) Additional Concerns

EA licensing is appealing because it provides simple, clear freedom to operate with one stroke of the pen--the signing

of the original license between the university and its licensee. Of course, additional provisions could be added to an EA license to meet specific concerns of the university and licensee. For example, universities could ensure that only manufacturers with a certain demonstrated capacity to produce quality products can legally notify, by requiring notifiers to have a certification of Good Manufacturing Practices (GMP) [FN314] or other guarantee of quality. [FN315] This would involve the university in a broader effort to police the actions of generic companies, creating obstacles where there are no established quality assessment standards. The same objective might be achieved more easily through an indemnification and insurance requirement, which universities may well wish to have in any case.

***1108** With some technologies, know-how and materials, which cannot be transferred under the freedom to operate model, may be an essential aspect of the rights a licensee uses to control production. [FN316] Any attempt to require affirmative transfer of materials or information from the licensee to a third party could raise some of the same enforcement challenges that a fair pricing approach would. There is no reason, in principle, that an EA license could not seek to bind a licensee to provide enabling know-how and associated materials reasonably necessary to the production of the end product. However, if a licensee violated the agreement, concerns over privity, in particular with respect to claims brought by an open and undefined class, suggest that it would often be left to the university to bring an enforcement action. [FN317]

Rather than providing a stark choice between enablement and litigation, an EA license might instead specify an intermediate step, requiring negotiations between all parties if enablement and transfer of materials were requested. In those cases where a university is concerned that products will only become available if the licensee itself produces them, it may not be able to avoid becoming involved in enforcement. It could then require transfers of know-how to third parties or seek to regulate the licensee's distribution diligence and pricing directly. This degree of individually negotiated requirements, monitoring, and enforcement may be beyond the resources and negotiating power of any individual university. If biologics become a much more important component of the pharmaceutical market, as some predict, [FN318] and generic companies are unable to readily reverse engineer them, effective pursuit of an EA strategy may require creation of a standing inter-university body charged with shepherding the performance and utilization of EA licenses. Modeled perhaps on PIPRA, ***1109** such a body would have to include a staff and collective funding mechanism and would be named specifically as an assignee of the university's rights under each EA license entered by a member university.

B. Addressing the R&D Gap: Implementing Neglected Disease Clauses and Innovative Partnerships

The EA licensing approach is designed to harness technologies developed through university technology transfers to industry. This approach will do little to address the lack of direct investment into research for neglected disease. Additional changes in the way that universities manage their IP portfolios can reduce barriers to R&D in these areas.

1. Neglected Disease Exemptions

The first strategy universities can adopt is one we term Neglected Disease (“ND”) licensing. If a university chooses to enter into an exclusive license for a research tool (a practice that we do not mean to advocate by making this proposal), it can insert a specially tailored research exemption into the license. Utilizing the same notification structure as the EA provision, the ND clauses would grant scientists worldwide the freedom to engage in research to address neglected diseases using the licensed technology. Just as importantly, ND exemptions guarantee those who conduct this research the right to market resulting products in LMI countries. Such an exemption could be applied to all technologies useful in biomedical research, from research tools to compounds intended for end products. The ND exemption we propose utilizes an open licensing approach, like the EA license, and is similarly commons-based.

Our ND proposal draws on the model proposed by the PIPRA initiative [FN319] and adapts it to provide researchers and producers in LMI countries freedom to operate with biomedical research tools. Unlike the EA provisions, the ND clauses do not necessarily entail obtaining a cross-license from the licensee. Instead, the ND clauses simply must carve-out of any exclusivity granted to the university's licensee a set of provisions for freedom to operate pertaining to neglected diseases. Such a core clause specifies that, notwithstanding anything else in the agreement, the university retains the right to license use of its technology for research on neglected diseases anywhere in the world and for commercial purposes in LMI countries. In this case, notification provided to the university alone will result in open licenses to conduct such activities. As with EA clauses, implementing an open licensing structure would minimize transaction costs ***1110** and allow any party to engage in research for a neglected disease after simple notification. A more robust model, which would more closely mirror the equitable access approach, would also capture all licensee improvements on the university's technology in the open licensing pool. [FN320] Critically, the ND clauses are not limited in geographical scope. Any entity is eligible to conduct research using the university's patented innovation--and if the more robust version is used, any licensee improvements to it--without paying a royalty, provided that the research targets a neglected disease.

Two approaches to defining the scope of the ND research exemption are possible. First, uses could be limited to academic institutions and other nonprofit entities (such as the Drugs for Neglected Diseases Initiative) that have as their primary aim producing products predominantly for patient populations in developing countries. The second approach would allow any entity to make use of the exemption, but to carefully establish the universe of applicable diseases. An ND license could, for example, allow an open license to any institution, public or private, for research targeting any disease on a list included in the license. [FN321] A more comprehensive and flexible approach would be to provide a standard for identifying rare diseases and to grant an open license to any scientist working on any disease meeting that standard. Current U.S. law defines a rare condition as one with an incidence of less than 200,000 persons in the United States or for which there is no reasonable expectation of recouping the necessary R&D investment in the U.S. market. [FN322] The FDA makes available a cumulative ***1111** list of all drugs for such diseases, [FN323] including a number for diseases of particular significance in LMI countries. [FN324] By taking the United States' approach, universities would be adopting a widely accepted definition of indications for which markets fail to provide.

As noted above, in practice, the most significant IP barriers to research may result from potential exclusion from commercializing a resulting invention. Therefore, the most important part of an ND exemption may be the assurance of freedom to exploit any eventual product in LMI countries. This can be accomplished by guaranteeing freedom to operate vis-à-vis the licensed technology in LMI countries.

A researcher acting under the ND exemption we propose would not have the right to commercialize an end product in a high-income market, unless she negotiated the necessary cross-license(s). An ND clause might mandate that the licensee receive an option for a cross-license for all high-income markets. Such a provision would likely appeal to licensees, and would ensure that the end product would not be barred from high-income markets on account of failed cross-licensing negotiations. However, avoiding such a mandate might provide greater incentives for private firms to engage in the relevant research.

Critics may express concern that the contractual creation of a worldwide neglected research exemption--both for the underlying university patent and any licensee or sublicense improvements--will actually lead to scientists using these technologies in research on non-neglected diseases. However, such research is not authorized by an ND clause, and would constitute actionable infringement. The pertinent question is whether ND uses can readily be distinguished from other uses in an infringement context. We argue that ND uses can be distinguished in the ways that matter most, and that where they cannot, little harm is done. When a drug is registered with a regulatory agency, any misuse of the ND re-

search exemption would likely become apparent. Of course, even with researchers acting in good faith, early-stage research may produce results applicable to a variety of indications, including non-neglected diseases. The ND exemption does not prevent a researcher from negotiating cross-licenses in order to exploit such an innovation. Where, on the other hand, the attempt to license***1112** or patent an innovation does not reveal the infringement, the infringement is likely of the class that is difficult to detect, and thus commonplace even in an environment without ND licensing.

2. Promoting Partnerships

The second component of universities' neglected disease agenda would be a more proactive approach to out-licensing of research tools. Universities need not wait until they exclusively license a technology to ensure that the technology is available to researchers working on neglected diseases. Universities can affirmatively grant scientists royalty-free licenses to use their tools for commercial and noncommercial research. This might be facilitated by the creation of simple, ready-to-sign agreements that could be posted on a TTO's website.

Universities can also seek out opportunities to license to public-private partnerships, and try to bring foundations into the agreement to provide support for the development of the technology. [FN325] Again, such initiatives should not be limited to attempts to produce medicines, but should also include diagnostics. [FN326] Finally, universities should explore the option of licensing early-stage inventions directly to entities in LMI countries that have the ability and desire to commercialize products for both neglected and non-neglected diseases. [FN327] Such agreements might sometimes offer limited forms of geographical exclusivity or co-exclusivity, [FN328] or leverage public or foundation financing to support the development of the technology. Such partnerships have many potential benefits. For example, they could help meet goals of development and technology transfer, and make use of the relatively low cost of research in LMI countries. [FN329]

***1113** C. Intersections Between EA Clauses, ND Clauses, and Partnerships

These approaches can, of course, be combined. EA and ND clauses can be implemented together to ensure freedom for suppliers of an eventual end product in LMI countries as well as freedom for researchers in high-income countries who seek to develop the compound for use against a neglected disease. [FN330] Similarly, EA clauses can be inserted into ND licenses to ensure that any resulting products must be licensed under terms that guarantee generic companies freedom to operate in LMI countries. Finally, when licensing to a nonprofit entity such as OneWorld Health, universities could adopt either EA or ND clauses. [FN331] Exactly how and when to supplement one approach with another will likely depend on the particular technologies and partners in question.

VI CONCLUSION

We have highlighted a series of institutional innovations that could constitute the backbone of a new agenda for access to biomedical innovations and research on treatments for neglected diseases. One strong advantage of our approach is that it can be undertaken in the absence of any changes to national or international IP regimes. By collectively adopting such an agenda, as well as clear and binding policies governing the use of these approaches, universities can maximize their joint potential to close the R&D and access gaps and improve the lives of people living in LMI countries. No one--not pharmaceutical companies, not patients in developed nations, and not universities--benefits from letting people in poor countries die from conditions that could be prevented or treated.

***1114** We must find ways around the many myopic and technical stumbling blocks that contribute to millions of pre-

ventable deaths each year. In the best case scenario, this voluntary solution will pave the way for IPR disarmament among a wide range of actors both in the United States and elsewhere--including universities, scientists, federal legislators, federal agencies, nonprofit drug development companies, and the pharmaceutical industry itself. On the other hand, there may be no spillover effects beyond providing access to university-generated medicines and research tools. Perhaps only a small percentage of research on neglected diseases is redirected, abandoned, or delayed because of problems accessing research tools. Perhaps patent-based costs account for only a few percent of preventable deaths from diseases in low- and middle-income countries. Perhaps open access to university-based technologies would only avert a fraction of these deaths and free up a fraction of the research tools relevant to neglected diseases. But preventing even a fraction of one percent of deaths in low- and middle-income countries would translate into saving tens of thousands of lives every year. The opportunity to prevent these deaths is a worthy goal for the community of scientists and universities to pursue, and to pursue together.

[FNd1]. Post-Doctoral Fellow in Law and Public Health, Yale Law School, Yale School of Public Health.

[FNdd1]. J.D. candidate, Yale Law School; Steering Committee, Universities Allied for Essential Medicines.

[FNddd1]. J.D. candidate, Yale Law School.

[FNdddd1]. Professor of Law, Yale Law School.

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[FN1]. See, e.g., World Health Org., World Health Report 2002, at 186-91.

[FN2]. UNAIDS, AIDS Epidemic Update 1 (Dec. 2004) [hereinafter UNAIDS 2004], http://www.unaids.org/wad2004/EPI_1204_pdf_en/EpiUpdate04_en.pdf.

[FN3]. World Health Org., Key Facts from the World Health Report 2004, at 1, http://www.who.int/whr/2004/en/facts_en.pdf.

[FN4]. In the United States, in the two years after ARVs were adopted for widespread use, AIDS-related mortality dropped by more than seventy percent. See Frank J. Palella et al., Declining Morbidity and Mortality Among Patients with Advanced Human Immunodeficiency Virus Infection, 338 New Eng. J. Med. 853 (1998); see also Paulo R. Teixeira et al., The Brazilian Experience in Providing Access to Antiretroviral Therapy, in Economics of AIDS and Access to HIV/AIDS in Developing Countries 69 (2003) (describing a similarly dramatic reduction in mortality in Brazil following the introduction of ARV therapy).

[FN5]. Approximately ninety-five percent of AIDS-related deaths occur in the developing world. See UNAIDS, AIDS Epidemic Update 5 (Dec. 2003), http://

www.unaids.org/html/pub/publications/irc-pub06/jc943-epiupdate2003_en_pdf.pdf. In 2001, a survey of seventy low-income countries found that only two percent of those with advanced HIV infection had access to treatment. Int'l HIV Treatment Access Coalition, World Health Org., A Commitment to Action for Expanded Access to HIV/AIDS Treatment 2 (2002). The following year, the World Health Organization (WHO) reported that on average only five percent of all people in need of ARVs worldwide received them; within sub-Saharan Africa, just one percent were treated. Int'l HIV Treatment Access Coalition, supra, at 1.

[FN6]. See Médecins Sans Frontières, Untangling the Web of Price Reductions: A Pricing Guide for the Purchase of ARVs for Developing Countries 9 (7th ed. 2005) [hereinafter MSF, Untangling the Web], http://www.accessmed-msf.org/documents/untanglingtheweb%207.pdf. At the same time, in Brazil, generics were being produced for less than $3000 per patient per year. Id.

[FN7]. Id.

[FN8]. A number of national ARV programs explicitly rely on generics. See, e.g., Charles Wendo, Uganda Begins Distributing Free Antiretrovirals, 363 Lancet 2062 (2004). International agencies have also found generics important to their program objectives. See Asia Russell, The Bush Administration's Global AIDS Promises--and Praxis, 4 Yale J. Health Pol'y L. & Ethics 133, 138 (2004) (citing Global Fund To Fight AIDS, Tuberculosis, & Malaria, Guidelines for Proposals (2003)); Keith Alcorn & Theo Smart, Fixed Dose ARV Combinations: Choices and Challenges, HIV & AIDS Treatment in Practice (NAM, United Kingdom, Mar. 2004) (noting that the WHO's 3 x 5 Initiative favors generics because they are believed to make the program affordable), at http:// www.aidsmap.com/en/docs/3FE6E952-3B09-494A-96E0-200381027DA0.asp; cf. Juan Rovira, Trade Agreements, Intellectual Property, and the Role of the World Bank in Improving Access to Medicines in Developing Countries, 4 Yale J. Health Pol'y L. & Ethics 401 (2004).

[FN9]. The programs are, however, headed in the right direction. The number of people in developing countries receiving treatment purportedly increased by nearly two-thirds in the second half of 2004. Compare Press Release, WHO/UNAIDS/Global Fund/U.S. Government, 700,000 People Living with AIDS in Developing Countries Now Receiving Treatment (Jan. 26, 2005), http:// www.who.int/mediacentre/news/releases/2005/pr07/en/print.html, with UNAIDS 2004, supra note 2, at 5 (reporting that 440,000 low- and middle-income country residents were receiving treatment as of June 2004, according to WHO statistics).

[FN10]. In the pharmaceutical field, patents are increasingly supplemented by other exclusive rights, such as rights in regulatory data. For the sake of clarity, this Article will refer to the range of patent and patent-like exclusive rights that may apply to medical technology collectively as “patent rights.” Also, when we discuss these exclusive rights we refer to them as they are usually used--that is, to secure a monopoly and extract supra-marginal returns.

[FN11]. We include the range of non-pharmaceutical products important to the practice of medicine, such as vaccines, diagnostics, and monitoring tools, when referring to medicines or medical or biomedical technologies.

[FN12]. See Jennifer Barrett, A Major Step, Newsweek (Web Exclusive), Nov. 24, 2003, at http://msnbc.msn.com/id/3606125; see also Edwin Cameron, The Deafening Silence of AIDS, 5 Health & Hum. Rts. 7 (2000) (describing the lack of access to treatment in South Africa in 2000).

[FN13]. Cf. Barrett, supra note 12 (mentioning Mbeki's refusal to accept that anti-retrovirals worked, as well as his subsequent reversal on the issue).

[FN14]. MSF and others have succeeded in establishing this principle. See Paul Farmer et al., Community-Based Approaches to HIV Treatment in Resource-Poor Settings, 358 Lancet 404 (2001); Toby Kasper et al., Demystifying Antiretroviral Therapy in Resource-Poor Settings, 32 Essential Drugs Monitor 20 (2003); Donald G. McNeil Jr., Africans Outdo U.S. Patients in Following AIDS Therapy, N.Y. Times, Sept. 3, 2003, at A1.

[FN15]. Letter from Eric Goemaere, Representative of Médecins Sans Frontières--South Africa, to Jon Soderstrom, Managing Director, Office of Cooperative Research, Yale University (Mar. 9, 2001) [hereinafter Goemaere MSF Letter] (on file with authors).

[FN16]. Id.; see also Melody Petersen, Lifting the Curtain on the Real Costs of Making AIDS Drugs, N.Y. Times, Apr. 24, 2001, at C1 (noting that Cipla, an Indian generic company, had offered to sell generic stavudine to health organizations for $40 per year).

[FN17]. Bristol-Myers Squibb brought the drug (also known as d4t) to market in 1994 under the brand name Zerit. See John Curtis, Hunting Down HIV, Yale Med., Summer 1998, http://info.med.yale.edu/external/pubs/ym_su98/cover/cov_hunting11.html

[FN18]. Goemaere MSF Letter, supra note 15.

[FN19]. We use the terms “patent-based,” “originator,” or “proprietary” to denote pharmaceutical companies, including biotech firms, that develop, produce, and/or market patented medicines. The Pharmaceutical Research and Manufacturers of America (PhRMA) represents the interests of these companies in the United States, and “PhRMA companies” is another common synonym. These terms specifically exclude generic companies, both in the developed and developing worlds.

[FN20]. See infra notes 150-54 and accompanying text.

[FN21]. See infra note 160.

[FN22]. See Medicines and Related Substances Control Amendment Act, No. 90 (1997) (S. Afr.); see also Mark Heywood, Debunking ‘Conglomo-Talk’: A Case Study of the Amicus Curiae as an Instrument for Advocacy, Investigation and Mobilization, Paper Presentation at Health, Law and Human Rights: Exploring the Connections Conference 13 (Sept. 29, 2001), http:// www.tac.org.za/Documents/MedicineActCourtCase/Debunking_Conglomo.rtf.

[FN23]. Cf. Barton Gellman, A Turning Point That Left Millions Behind, Wash. Post, Dec. 28, 2000, at A1 (citing the Chairman of Pfizer, in 2000, who argued in favor of a donation program in developing countries, instead of differential pricing or generic competition, for its important AIDS drug diflucan because the industry “lives and dies on intellectual property”).

[FN24]. See Press Release, Bristol-Myers Squibb, Bristol-Myers Squibb Announces Accelerated Program To Fight HIV/AIDS in Africa (Mar. 14, 2001), http://www.prnewswire.co.uk/cgi/news/release?id=64424. While a steep discount, this price was still higher than the price offered by generic companies. See Goemaere MSF Letter, supra note 15. Generic forms of stavudine have been available in South Africa since 2003, and two companies have been awarded a tender to supply generic d4t to the South African government. See Amy Kapczynski et al., Editorial, Global Health and University Patents, 300 Science 1629 (2003); South African Generic Drug Maker To Produce Country's First Generic Antiretroviral Drug, Kaiser Daily HIV/AIDS Rep., Aug. 7, 2003, at http://kaisernetwork.org/daily_reports/rep_index.cfm?hint=1&DR_ID=19240; Press Release, South Africa Department of

Health, ARV Drug Tender Awarded (Mar. 3, 2005), http://www.doh.gov.za/docs/pr/pr0303-f.html.

[FN25]. See, e.g., Karen DeYoung & Bill Brubaker, Another Firm Cuts HIV Drug Prices, Wash. Post, Mar. 15, 2001, at A1; Michael Waldholz & Rachel Zimmerman, Bristol-Myers Offers To Sell Two AIDS Drugs in Africa at Below Cost, Wall St. J., Mar. 15, 2001, at B1.

[FN26]. See Rachel L. Swarns, Drug Makers Drop South Africa Suit over AIDS Medicine, N.Y. Times, Apr. 20, 2001, at A1.

[FN27]. See, e.g., Drug Company Cuts AIDS Drug Prices in S. Africa, Reuters NewsMedia, Nov. 30, 2001, http://www.emro.who.int/asd/WhatsNew-GlobalEvents-Reuters3011.htm; Rachel Zimmerman & Michael Waldholz, Abbott To Cut Prices on AIDS Drugs Distributed in Sub-Saharan Africa, Wall St. J., Mar. 27, 2001, at A3

[FN28]. See, e.g., Press Release, Aspen Pharmacare Ltd., Aspen Pharmacare Receive Voluntary License from GlaxoSmithKline on Anti-Retroviral Patents in South Africa (Oct. 8, 2001) [hereinafter Aspen Pharmacare Press Release], http://www.aspenpharmacare.co.za/showarticle.php?id=135.

[FN29]. Treatment Action Campaign (TAC), a South African NGO, for example, aligned with the ruling African National Congress (ANC) party during the drug company lawsuit. Directly after the victory, the ANC made clear that it had no plans to take advantage of the potential for lower prices by creating a national treatment program. See Ben Hirschler, Glaxo Gives Up Rights to AIDS Drugs in South Africa, Reuters NewsMedia, Oct. 6, 2001 (describing the government's resistance and TAC's response), http:// www.aegis.com/news/re/2001/RE011009.html. TAC then shifted its focus to the government, filing and winning a landmark constitutional case establishing the government's obligation to create programs to provide medicines to HIV-positive women to prevent the transmission of HIV to their children. Minister of Health v. Treatment Action Campaign, 2002 (5) SALR 721 (CC) (S. Afr.). In 2003, the South African government finally launched a national antiretroviral program, employing generic stavudine as a key component of the formulary. See Julian Meldrum, South African HIV Treatment To Depend on Generic Drugs, AIDSmap News, Aug. 7, 2003, http://www.aidsmap.com/en/news/F5E96962-F1B4-40F2-8969-624AC8A7D424.asp. Approximately 27,000 people are reportedly now receiving treatment from the public sector. See Ben MacIennan, Aids Activists Are Govt's ‘Conscience’, Mail & Guardian (S. Afr.), Feb. 16, 2005, http:// www.mg.co.za/articlePage.aspx?articleid=197660&area=/breaking_news/breaking_ news_national. While this represents a significant advance, it remains far shy of the government's announced intention to treat 50,000 people by the end of 2004. See Sharon LaFraniere, South Africa Approves Plan To Offer Free AIDS Medication, N.Y. Times, Nov. 20, 2003, at A3.

[FN30]. There is no standard definition of “neglected diseases,” and other terms such as tropical diseases or developing-country diseases are often used interchangeably.

[FN31]. United Nations Dev. Programme, Incentives To Reduce the 10/90 Gap (2002), http://www.undp.org/ods/monterrey-sideevent/incentive.pdf; see Global Forum for Health Research, The 10/90 Report on Health Research 2003-2004 (2004).

[FN32]. See Drugs for Neglected Diseases Initiative, Sleeping Sickness (Human African Trypanosomiasis), at http://www.dndi.org/cms/public_ html/insidearticleListing.asp? CategoryId=89&SubCategoryId=147&ArticleId=201&TemplateId=1 (last visited Apr. 8, 2005).

[FN33]. These country classifications are made by the World Bank. See World Bank Group, Data and Statistics: Country

Classification, at http:// www.worldbank.org/data/countryclass/countryclass.html (last visited Apr. 28, 2005); World Bank Group, Data and Statistics: Country Groups, at http:// www.worldbank.org/data/countryclass/classgroups.htm (last visited Apr. 28, 2005). In 2002, "94.9% of the global sales of the U.S.-based brand-name pharmaceutical industry came from the U.S., Canada, Europe (including Eastern Europe and Russia), Japan, Australia and New Zealand." William W. Fisher & Talha Syed, Patent Law, Drugs and the Health Crisis in the Developing World 76-77 (Feb. 24, 2005) (unpublished manuscript, on file with authors). The most recent report from the pharmaceutical industry's trade association, PhRMA, offers data that support the conclusion that LMI markets contribute five to seven percent of sales. See Pharm. Research & Mfrs. of Am., Pharmaceutical Industry Profile 2005--From Laboratory to Patient: Pathways to Biopharmaceutical Innovation 40 (2005) (including Latin America, Asia-Pacific-- except Japan, India, and Pakistan--Central and Eastern Europe, Russia, and the Middle East in the estimation of LMI markets). PhRMA members represent a very large proportion of the patent-based industry, and of U.S. firms engaged in R&D. Its data is thus well-tailored for the purposes of this Article, and we are grateful to Talha Syed for directing us to it.

[FN34]. This percentage was steady between 2002 and 2004, according to IMS Health. See Press Release, IMS Health, IMS Reports 2004 Global Pharmaceutical Sales Grew 7 Percent to $550 Billion (Mar. 9, 2005) (indicating the percent did not change from 2003 to 2004), http:// www.imshealth.com/ims/portal/front/articleC/0,2777,6599_3665_71496463,00.html; Press Release, IMS Health, IMS Reports 8 Percent Constant Dollar Growth in 2002 Audited Global Pharmaceutical Sales to $400.6 Billion (Feb. 25, 2003), http:// www.imshealth.com/ims/portal/front/articleC/0,2777,6599_3665_41336931,00.html. Australia, which is of course not an LMI country, is likely a somewhat significant share of this percentage, but IMS Health does not publicly provide these percentages disaggregated by country. The main distinction between this and PhRMA data is due to IMS Health's inclusion of generic sales.

[FN35]. While our proposals could be adopted by nonprofits, universities, and even private firms both within and outside of the United States, we concentrate our discussion on U.S. universities.

[FN36]. See Yochai Benkler, Commons-Based Strategies and the Problems of Patents, 305 Science 1110 (2004).

[FN37]. See, e.g., Elinor Ostrom, Governing the Commons: The Evolution of Institutions for Collective Action (1990); Carol Rose, The Comedy of the Commons: Custom, Commerce, and Inherently Public Property, 53 U. Chi. L. Rev. 711 (1986).

[FN38]. Open source or free software innovation has attracted significant academic attention, as has peer production of other types of information, knowledge, and culture more generally. See Steven Weber, The Success of Open Source (2004); Josh Lerner & Jean Tirole, The Scope of Open Source Licensing, 21 J.L. Econ. & Org. 20 (2005); Eric von Hippel & Georg von Krogh, Open Source Software and the Private-Collective Innovation Model: Issues for Organization Science, 14 Org. Sci. 209 (2003).

[FN39]. See, e.g., Yochai Benkler, Coase's Penguin, or, Linux and The Nature of the Firm, 112 Yale L.J. 369 (2002).

[FN40]. See, e.g., Yochai Benkler, Sharing Nicely: On Shareable Goods and the Emergence of Sharing as a Modality of Economic Production, 114 Yale L.J. 273 (2004).

[FN41]. We define an "open" licensing provision as one that is available to everyone on the same terms. In this sense open licensing is not the same as dedication to the public domain. A self-reinforcing licensing approach that employs patent and other rights--rather than simply dedicating innovations to the public domain--may be necessary to sustain a commons where key institutional players, including national governments and private-sector firms, are intent on promot-

ing the expansion and utilization of exclusive rights.

[FN42]. EA licensing is not truly an “open source” strategy--a term that describes software for which source code is made freely available to independent software developers. Nonetheless, it mimics open source software's approach to IPRs by ensuring that the licensed technology and subsequent developments remain freely available to all potential users under an EA license. While other open licensing models typically offer the freedom to operate in all markets, including high income markets, our proposal is restricted to low- and middle-income settings.

[FN43]. See James Boyle, The Second Enclosure Movement and the Construction of the Public Domain, 66 Law & Contemp. Probs. 33, 39 (2003).

[FN44]. In 1980, the Supreme Court held that genetically engineered microorganisms could be patented. Diamond v. Chakrabarty, 447 U.S. 303 (1980). In 1988, the Patent and Trademark Office (PTO) granted its first patent on a four-legged animal, Harvard University's OncoMouse. See U.S. Patent No. 4,736,866 (issued Apr. 12, 1988). Currently, the PTO regularly grants patents on isolated and purified versions of naturally occurring DNA fragments and other biological compounds. See Linda J. Demaine & Aaron Xavier Fellmeth, Reinventing the Double Helix: A Novel and Nonobvious Reconceptualization of the Biotechnology Patent, 55 Stan. L. Rev. 303, 304 (2002).

[FN45]. Rebecca S. Eisenberg, Patents, Product Exclusivity, and Information Dissemination: How Law Directs Biopharmaceutical Research and Development, 72 Fordham L. Rev. 477, 481 (2003).

[FN46]. Scholars have referred to such rights as a second line of patent protection. See, e.g., id. at 482-83. In the United States, for example, data associated with new drugs receive five years of exclusive protection, while data associated with a new indication of an existing drug receive three years of exclusive protection. 21 U.S.C. §355(c)(3)(E)(ii)-(iii) (2000). This trend has been exported through provisions in trade agreements that require strict protection of pharmaceutical test data. See Susan Scafidi, The “Good Old Days” of TRIPS: The U.S. Trade Agenda and the Extension of Pharmaceutical Test Data Protection, 4 Yale J. Health Pol'y L. & Ethics 341 (2004).

[FN47]. See Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C art. 27.1, Legal Instruments--Results of the Uruguay Round vol. 31, 33 I.L.M. 81 (1994) [hereinafter TRIPS Agreement]. Least-developed countries have until January 1, 2006, to comply with TRIPS and have the right to defer patents and data exclusivity rights on pharmaceuticals until 2016. World Trade Org., Doha WTO Ministerial 2001, Declaration on the TRIPS Agreement and Public Health, WT/MIN(01)/DEC/2, P7 (Nov. 20, 2001) [hereinafter Doha Declaration] (amending the timeline for implementation); Press Release, World Trade Org., Council Approves LDC Decision with Additional Waiver (June 28, 2002), http://www.wto.org/english/news_e/pres02_e/pr301_e.htm. For a discussion of the TRIPS Agreement and the actors behind it, see Peter Drahos with John Braithwaite, Information Feudalism: Who Owns the Knowledge Economy (2002), and Susan K. Sell, Private Power, Public Law: The Globalization of Intellectual Property Rights (2003). For a guide to the provisions of TRIPS, see Michael Blakeney, Trade Related Aspects of Intellectual Property Rights: A Concise Guide to the TRIPS Agreement (1996). For a consideration of the particular implications of the TRIPS Agreement for developing countries, see Carlos Correa, The TRIPs Agreement: A Guide for the South (1997).

[FN48]. See, e.g., Carsten Fink & Patrick Reichenmiller, Tightening TRIPS: The Intellectual Property Provisions of Recent US Free Trade Agreements (World Bank Group, Int'l Trade Dep't, Trade Note 20, 2005). The European Union has also used free trade agreements to impose TRIPS-plus requirements upon countries. See Pradeep S. Mehta et al., “TRIPs-Plus”: Enhancing Right Holders' Protection, Eroding TRIPs' Flexibilities (CUTS Centre for Int'l Trade, Econ., and Env't., Briefing Paper No. 2, 2004). Regional agreements also sometimes impose standards higher than those in the

TRIPS Agreement, as is the case for the Bangui Agreement among the African Intellectual Property Organization (OAPI) countries of West Africa. See [Gr. Brit.] Comm'n on Intellectual Prop. Rights, Integrating Intellectual Property Rights and Development Policy 8 (2002) [hereinafter Comm'n on IPR], http:// www.iprcommission.org/papers/pdfs/final_report/CIPRfullfinal.pdf; Ellen 't Hoen, TRIPS, Pharmaceutical Patents, and Access to Essential Medicines: A Long Way from Seattle to Doha, 3 Chi. J. Int'l L. 27, 45 (2002).

[FN49]. See Drahos with Braithwaite, supra note 47, at 85-149 (discussing the history of TRIPS); Sell, supra note 47, at 96 (noting that through TRIPS, "[i]n effect, twelve corporations made public law for the world").

[FN50]. See Carlos Correa, Integrating Public Health Concerns into Patent Legislation in Developing Countries 11 (2000) (citing United Nations Conference on Trade and Development, The TRIPs Agreement and Developing Countries, New York and Geneva (1996)), http:// www.southcentre.org/publications/publichealth/publichealth-04.htm.

[FN51]. See, e.g., Rovira, supra note 8, at 401 n.3; see also John H. Barton, TRIPS and the Global Pharmaceutical Market, 23 Health Aff. 146, 148-49 (2004) ("[T]he logic of the patent system is to permit an elevated price to allow recovery of research and development (R&D) costs.").

[FN52]. For a brief review of some of the relevant views in economics, see Frederick M. Abbott, The TRIPS Agreement, Access to Medicines and the WTO Doha Ministerial Conference 6 (Quaker U.N. Office, Occasional Paper 7, 2001).

[FN53]. Kenneth Arrow articulated this basic tradeoff between rights, innovation, and welfare over forty years ago. See Kenneth J. Arrow, Economic Welfare and the Allocation of Resources for Invention, in The Rate and Direction of Inventive Activity: Economic and Social Factors 609, 614-15 (Nat'l Bureau of Econ. Research ed., 1962).

[FN54]. See, e.g., Josh Lerner, Patent Protection and Innovation Over 150 Years (Nat'l Bureau Econ. Research, Working Paper No. 8977, 2002); see also Adam B. Jaffe & Josh Lerner, Innovation and Its Discontents: How Our Broken Patent System Is Endangering Innovation and Progress, and What To Do About It 16-18 (2004); Arrow, supra note 53, at 616-17.

[FN55]. See, e.g., Joshua D. Sarnoff, Abolishing the Doctrine of Equivalents and Claiming the Future After Festo, 19 Berkeley Tech. L.J. 1157, 1209 (2004) (noting that although "[s]ubstantial evidence points to the increasingly weak incentives that patents provide relative to other mechanisms for protecting innovations and investments, ... patent protection may be important to particular technology sectors (such as the pharmaceutical and software industries)").

[FN56]. See, e.g., Richard C. Levin et al., Appropriating the Returns from Industrial Research and Development, 1987 Brookings Papers on Econ. Activity 783, 796.

[FN57]. See, e.g., Nancy Gallini & Suzanne Scotchmer, Intellectual Property: When Is It the Best Incentive System?, in 2 Innovation Policy and the Economy 51 (Adam B. Jaffe et al. eds., 2001); Brian D. Wright, The Economics of Invention Incentives: Patents, Prizes, and Research Contracts, 73 Am. Econ. Rev. 691 (1983).

[FN58]. See, e.g., Aidan Hollis, An Efficient Reward System for Pharmaceutical Innovation 4-9 (Jan. 17, 2005), http://econ.ucalgary.ca/fac-files/ah/drugprizes.pdf. Hollis summarizes the problem with the traditional consensus in support of patent-driven pharmaceutical R&D this way: "Because pharmaceutical markets function poorly, the patent system does not effectively stimulate drug research and development. Instead, it induces large amounts of research into drugs with relatively little incremental therapeutic value, while providing inadequate incentives to innovate in some areas of great therapeutic value." Id. at 1. He proposes, instead, a prize-based system that would reward inventors according to

the incremental therapeutic benefit offered by their inventions. Id.; see also Medical Innovation Prize Act of 2005, H.R. 417, 109th Cong. (2005) (proposing, with regard to medical products, to replace the patent system with a prize fund); Michael Kremer, Pharmaceuticals and the Developing World, J. Econ. Persps., Fall 2002, at 67, 82 (advocating, with regard to "products needed primarily by developing countries," advance purchase commitments to reward research outputs).

[FN59]. World Health Org., Equitable Access to Essential Medicines: A Framework for Collective Action 1 (2004) [hereinafter WHO, Framework for Action]. The WHO defines essential medicines as "those that satisfy the priority health care needs of the population." World Health Org., Essential Drugs and Medicines Policy, at http://www.who.int/medicines (last updated Mar. 3, 2005). The WHO's essential drugs list (EDL) is compiled by an Expert Committee, on the basis of a variety of factors including "the disease burden and sound and adequate data on the efficacy, safety and comparative cost-effectiveness of available treatments." World Health Org., Procedure to Update and Disseminate the WHO Model List of Essential Medicines, Document EB109/8 (Annex), Dec. 7, 2001, http://www.who.int/medicines/organization/par/edl/procedures.shtml (last updated July 28, 2004). While the EDL is useful for many purposes, it is important to note that it is not a list of all life-saving medicines, much less all medicines that would provide medical benefit to individuals in developing countries.

[FN60]. See WHO, Framework for Action, supra note 59, at 1.

[FN61]. Jonathan Quick of the WHO's Essential Medicines Division identifies four: "(1) irrational use of medicines, (2) unfair financing for healthcare, including medicines, (3) unreliable delivery systems and (4) high medicines prices." Jonathan D. Quick, Editorial, Essential Medicines Twenty-Five Years On: Closing the Access Gap, 18 Health Pol'y & Plan. 1, 1 (2003); see Hannah E. Kettler & Chris Collins, Using Innovative Action To Meet Global Health Needs Through Existing Intellectual Property Regimes 40 (Comm'n on Intellectual Prop. Rights, Study Paper 2b, 2004) (identifying "[f]inancial resources, health care infrastructure, and political will" as some of the pivotal factors), http://www.iprcommission.org/papers/pdfs/study_papers/sp2b_kettler_study.pdf.

[FN62]. Many existing drugs are unaffordable for patients around the world. See, e.g., MSF, Untangling the Web, supra note 6, at 4 (noting that "[t]he high price of HIV/AIDS medicines continue[s] to represent one of the main barriers to their availability in developing countries," citing in particular the high cost of second-line therapies for drug resistant HIV). Price is not just a problem for people living with HIV/AIDS. The high cost of interferon/ribavrin combination therapy for Hepatitis C is "unquestionably beyond the reach of developing countries." Médecins Sans Frontières, Doha Derailed: A Progress Report on TRIPS and Access to Medicines 6 (2003), http://www.accessmed-msf.org/documents/cancunbriefing.pdf. Access to other drugs, from certain classes of antibiotics to anti-cancer drugs, has also been limited by price. See, e.g., id.; Nadia Aït-Khaled et al., Chronic Respiratory Diseases in Developing Countries: The Burden and Strategies for Prevention and Management, 79 Bull. World Health Org. 971 (2001) (describing need for low-cost generic alternatives to treat asthma in developing countries); Mogha Kamal Smith, Why Developing Countries Need Access to Cheap Treatments for Diabetes, Diabetes Voice, July 2003, at 31, 32 (noting that only three percent of people with diabetes in developing countries get treatment "partly because the majority of these people have to pay for their drugs out of their own pockets"); Thousands Denied Anti-Cancer Drugs, BBC News, Feb 14, 2003 (citing price as a major barrier to access to cancer drugs in developing countries), at http://news.bbc.co.uk/2/hi/health/2761277.stm. High prices also constitute a barrier to the drugs that do exist for neglected diseases. See Rachel Cohen, An Epidemic of Neglect, Multinational Monitor, June 2002, http:// multinationalmonitor.org/mm2002/02june/june02corp1.html; Médecins Sans Frontières, The Campaign: Target Diseases, Leishmaniasis, at http:// www.accessmed-msf.org/campaign/lsh01.shtm (last visited Mar. 9, 2005) (describing lack of access to treatment in countries where there is no generic available); Médecins Sans Frontières, The Campaign: Target Diseases, Sleeping Sickness, at http://www.accessmed-msf.org/campaign/slp01.shtm (last visited Mar. 9, 2004) (describing severe lack of

access to diagnostics and treatment for African sleeping sickness).

[FN63]. Comm'n on IPR, supra note 48, at 37 (citing several studies about the specific and very positive effects that price cuts on ARVs would have upon consumption in countries like Uganda). This is especially the case for the poor. See Adam Wagstaff & Mariam Claeson, World Bank, The Millennium Development Goals for Health: Rising to the Challenges 9 (2004) ("Higher money prices tend to reduce demand--especially among the poor--unless accompanied by improvements in service quality."); Wagstaff & Claeson, supra, at 75 ("Affordability--the price paid relative to discretionary income--is undoubtedly one important barrier preventing the use of health services.").

[FN64]. See Quick, supra note 61, at 2-3 ("[G]overnments, other health care providers, and households in developing countries are each highly sensitive to medicines prices."). In LMI countries, high drug prices have been shown to have devastating results for the poor. For example, in Vietnam in 1993, just one visit by an individual in a household in the poorest fifth of the population to a local health center "resulted in a bill for drugs equal to 11 percent of the household's annual nonfood consumption." Wagstaff & Claeson, supra note 63, at 119 box 7.9. As many as three million Vietnamese have been "pushed into poverty as a result of high out-of-pocket payments for healthcare, much of it attributable to high drug costs." Wagstaff & Claeson, supra note 63, at 119 box 7.9. Households also "appear to have been deterred from using health services because of high drug costs." Wagstaff & Claeson, supra note 63, at 119 box 7.9.

[FN65]. WHO, Framework for Action, supra note 59, at 1; see Jonathan D. Quick, Ensuring Access to Essential Medicines in the Developing Countries: A Framework for Action, 73 Clinical Pharmacology & Therapeutics 279, 282 (2003) ("Private out-of-pocket spending on medicines is the largest household health expenditure in many [developing] countries ...."). By comparison, "in many high income countries, over 70% of pharmaceuticals are publicly funded." WHO, Framework for Action, supra note 59, at 1.

[FN66]. WHO, Framework for Action, supra note 59, at 5 (noting that median insurance coverage "is 35% in Latin America, 10% in Asia, and less than 8% in Africa" and that "the inclusion of medicine reimbursement in health insurance varies greatly").

[FN67]. See World Health Org., The World Medicines Situation 46 tbl.5.3 (2004) [hereinafter WHO, World Medicines Situation].

[FN68]. .Comm'n on IPR, supra note 48, at 37. Developing countries newly introducing patents also are disadvantaged by the fact that the resulting profits are likely to accrue mostly to companies outside the country. See Jean O. Lanjouw, The Introduction of Pharmaceutical Product Patents in India: "Heartless Exploitation of the Poor and Suffering?" 5-6 (Nat'l Bureau Econ. Research, Working Paper No. 6366, 1998).

[FN69]. Médecins Sans Frontières et al., Surmounting Challenges: Procurement of Antiretroviral Medicines in Low- and Middle-Income Countries 46 (2003), http://www.accessmed-msf.org/documents/procurementreport.pdf.

[FN70]. See Mohga K. Smith, Generic Competition, Price, and Access to Medicines: The Case of Antiretrovirals in Uganda 2 (Oxfam Briefing Paper No. 26, 2002).

[FN71]. See Amir Attaran, How Do Patents and Economic Policies Affect Access to Essential Medicines in Developing Countries?, 23 Health Aff. 155 (2004); see also Amir Attaran & Lee Gillespie-White, Do Patents for Antiretroviral Drugs Constrain Access to AIDS Treatment in Africa?, 286 JAMA 1886, 1888 tbl.1 (2001).

[FN72]. See, e.g., Comm'n on IPR, supra note 48, at 20-26, 29-51; Kevin Outterson, Pharmaceutical Arbitrage: Balan-

cing Access and Innovation in International Prescription Drug Markets, 5 Yale J. Health Pol'y L. & Ethics 193, 255-58 (2005).

[FN73]. Many of the most important ARVs, for example, are widely patented in Africa. See Marleen Boelaert et al., Letter to the Editor, Do Patents Prevent Access to Drugs for HIV in Developing Countries?, 287 JAMA 840 (2002); Consumer Project on Technology et al., Comment on the Attaran/Gillespie-White and PhRMA Surveys of Patents on Antiretroviral Drugs in Africa (Oct. 16, 2001), at http://www.cptech.org/ip/health/africa/dopatentsmatterinafrica.html; see also infra note 160 (noting GlaxoSmithKline's attempt to prevent generic companies from selling cheaper versions of their ARV products in Ghana and Uganda).

[FN74]. See Attaran, supra note 71, at 158.

[FN75]. .See id. at Supplemental Exhibit, available at http:// content.healthaffairs.org/cgi/content/full/23/3/155/DC1. One example is Malawi, which has a per capita gross national income of less than $200 per year. Id.

[FN76]. Frederick M. Abbott, The WTO Medicines Decision: The Political Economy of World Pharmaceutical Trade and the Protection of Public Health, 99 Am. J. Int'l L. (forthcoming 2005) (manuscript of Mar. 31, 2005 at 28, on file with authors). Few developing countries can produce the essential active pharmaceutical ingredients (APIs), although if they are able to acquire APIs cheaply, many can formulate finished products. Id. (manuscript at 28 n.147) (noting that the APIs that make up ARV medicines are complex, and made only by a few companies in the world); see also WHO, World Medicines Situation, supra note 67, at 6 (reporting that only thirteen countries in the world make both formulations and APIs).

[FN77]. See, e.g., Robert Lewis-Lettington & Chikosa Banda, A Survey of Policy and Practice on the Use of Access to Medicines-Related TRIPs Flexibilities in Malawi 14 (2004) (noting that although Malawi has some capacity to make finished products, it imports APIs from India or China, and that "generic pharmaceutical products manufactured in Malawi are generally more expensive than those imported from elsewhere, for example, from India" because, inter alia, of high transportation costs, high communications costs, and limited markets), http://www.dfidhealthrc.org/Shared/publications/Issues_ papers/ATM/Lettington.pdf; see also Robert Lewis-Lettington & Peter Munyi, Willingness and Ability To Use TRIPs Flexibilities: Kenya Case Study 12-13 (2004) (reporting the same dynamics in Kenya), available at http:// www.dfid.gov.uk/pubs/files/dfidkenyareport.pdf.

[FN78]. See S. Africa's Aspen To Launch First Local AIDS Drug, Reuters NewsMedia, Aug. 5, 2003, http://www.aegis.com/news/re/2003/RE030806.html; see also Outterson, supra note 72, at 257.

[FN79]. See S. Africa's Aspen To Launch First Local AIDS Drug, supra note 78.

[FN80]. Some argue that patents are not a significant concern in developing countries because the WHO's EDL is mostly comprised of drugs that are off patent. See Attaran, supra note 71, 159-60. This argument ignores medicines not yet invented and the fact that medicines only appear on the EDL after an assessment that includes their "cost-effectiveness." See supra note 59.

[FN81]. See generally Médecins Sans Frontières & Drugs for Neglected Diseases Working Group, Fatal Imbalance--The Crisis in Research and Development for Drugs for Neglected Diseases (2002); Carlos M. Morel, Neglected Diseases: Under-funded Research and Inadequate Health Interventions, 4 EMBO Rep. S35 (2004); Ellen F.M. 't Hoen, The Responsibility of Research Universities To Promote Access to Essential Medicines, 3 Yale J. Health Pol'y L. & Ethics 293 (2003); Patrice Trouiller et al., Drug Development for Neglected Diseases: A Deficient Market and a Public-Health

Policy Failure, 359 Lancet 2188 (2002).

[FN82]. See Global Forum for Health Research, supra note 31.

[FN83]. Trouiller et al., supra note 81, at 2189-90; see Press Release, Médecins Sans Frontières, Drugs for Neglected Diseases Initiative: Teaming Up To Address Neglect (Mar. 12, 2003), http://www.accessmed-msf.org/prod/publications.asp?scntid =12320031354463&contenttype=PARA&. Public-sector-based research, particularly R&D sponsored by the military, has been an important source of drugs for diseases that have primary incidence in LMI countries. See, e.g., Donald G. McNeil Jr., Herbal Drug Widely Embraced in Treating Resistant Malaria, N.Y. Times, May 10, 2004, at A1 (discussing artemisinin, a treatment for malaria first isolated by Chinese military researchers, as well as mefloquine, an antimalarial drug developed at the Walter Reed Army Institute of Research in the 1960s).

[FN84]. Warren Kaplan & Richard Laing, World Health Org., PriorityMedicines for Europe and theWorld 62 (2004), http:// mednet3.who.int/prioritymeds/report/index.htm. Oxytocin is used to treat post-partum hemorrhage in women, which is a major cause of disability and death in developing countries. Id. at 47.

[FN85]. These would be especially useful for second-line ARVs and multidrug resistant tuberculosis. Id. at 124.

[FN86]. See, e.g., Renuka Rayasam, Austin-Based Company Will Build Device To Improve Treatment in Developing Countries, Austin Am. Statesman, July 9, 2004.

[FN87]. Few drug companies have tailored treatments to suit children with AIDS, in part because there are declining numbers of children born with HIV/AIDS in wealthy countries. See Editorial, Children and AIDS, N.Y. Times, Feb. 22, 2005, at A16. The market is apparently too small to attract even the modest investment needed to create low-dose, breakable, or chewable tablets. See Médecins Sans Frontières, Children and AIDS: Neglected Patients (July 15, 2004), http://www.msf.org/content/page.cfm?articleid=C35A2DA2-D4E3-425A-879860086416E313.

[FN88]. Rovira, supra note 8, at 405; see also Jean O. Lanjouw, Intellectual Property, and the Availability of Pharmaceuticals in Poor Countries, in 3 Innovation Policy and the Economy 91, 100 (Adam B. Jaffe et al. eds., 2003).

[FN89]. See, e.g., Lanjouw, supra note 68, at 7-8 (presenting this argument but also offering reasons that it may “paint[] too gloomy a picture”).

[FN90]. This cannot reasonably be attributed to a lack of patent protection or enforcement. See generally Lanjouw, supra note 88. Moreover, when research is oriented toward conditions affecting LMI populations, it tends to target those affecting the upper classes. See Emmanuel Combe et al., Pharmaceutical Patents, Developing Countries, and HIV/AIDS Research, in Economics of Aids and Access to HIV/AIDS Care in Developing Countries 151, 160 (2003).

[FN91]. See John P. Walsh et al., Research Tool Patenting and Licensing and Biomedical Innovation, in Patents in the Knowledge-Based Economy 285, 331 (Wesley M. Cohen & Stephen A. Merrill eds., 2003) (confirming that such patenting is increasing).

[FN92]. Michael A. Heller & Rebecca S. Eisenberg, Can Patents Deter Innovation? The Anticommons in Biomedical Research, 280 Science 698 (1998).

[FN93]. Carl Shapiro, Navigating the Patent Thicket: Cross-Licenses, Patent Pools, and Standard Setting, in 1 Innovation Policy and the Economy 119 (Adam B. Jaffe et al. eds., 2000). Shapiro describes a patent thicket as the “overlapping set

of patent rights requiring that those seeking to commercialize new technology obtain licenses from multiple patentees." Id. at 119.

[FN94]. See Walsh et al., supra note 91, at 314 (noting that more than one-third of respondents in the authors' survey of scientists, IP attorneys, and business managers reported that patents on research tools caused delays and added to the costs of research); see also John P. Walsh et al., Working Through the Patent Problem, 299 Science 1021, 1021 (2003) (noting that assertions of IP rights may hinder science and that policy makers should take steps to ensure continued protection of science intended for the public domain). But see David E. Adelman, A Fallacy of the Commons in Biotech Patent Policy, 20 Berkeley Tech. L.J. 985 (2005) (arguing that the potential adverse effects of biotech patenting are less significant than many have predicted).

[FN95]. See Walsh et al., supra note 91, at 286.

[FN96]. Arti K. Rai, Proprietary Rights and Collective Action: The Case of Biotechnology Research with Low Commercial Value, in International Public Goods and Transfer of Technology Under a Globalized Intellectual Property Regime 288, 289 (Keith E. Maskus & J.H. Reichman eds., forthcoming 2005); see also Walsh et al., supra note 91, at 304 (noting that transaction costs were only relevant when projects had questionable commercial viability).

[FN97]. See Rai, supra note 96, at 295-96 & nn.38-44 (discussing these problems in the context of a malaria vaccine and transgenic agricultural products relevant to developing countries). We might hope that companies would be more amenable to granting research licenses to low-commercial-value projects since these do not threaten the product markets that the company cares about. Cf. id. at 299-300 (suggesting that collective rights management has a better chance of success with low-commercial-value research). However, direct competition is only one of the concerns that such research may pose to the profits of a patent-holding firm. Another concern is the potential for follow-on research that might raise safety questions about a therapeutic compound. See infra note 103 and accompanying text.

[FN98]. See Walsh et al., supra note 91, at 286. Patents on compounds seem to trigger this response more often than do patents on research tools, but this is little comfort for those concerned with R&D for new medicines. Id. at 303 (reporting that "[o]f the 11 industry respondents who did mention IP as a cause for redirecting their research, seven ... were primarily concerned with IP on compounds, not on research tools").

[FN99]. See Eric G. Campbell et al., Data Withholding in Academic Genetics: Evidence from a National Survey, 287 JAMA 473, 479 (2002) (concluding that "[t]he commercial applications of genetics research, along with increasing dependence on industry funding and the rise of commercial norms in the academy may be partially responsible" for this withholding). Campbell et al.'s survey showed that over a three-year period, about half of geneticists polled had been unable to obtain information or materials from another university-based geneticist, and twenty-one percent had therefore abandoned a promising line of research. Id. at 478. In about twenty percent of the cases, one important reason cited for refusing to grant access to others was the need to abide by an agreement with an industrial sponsor or preserve confidentiality for patenting purposes. Although the most common reason given for such refusals was the "effort required," this category "probably also includes costs associated with difficulties in concluding complex negotiations over [Material Transfer Agreements]." Rai, supra note 96, at 294 (discussing Campbell et al.'s results).

[FN100]. See 35 U.S.C. §271 (2000).

[FN101]. Myriad Genetics has used its patents on genes that appear to trigger breast cancer to force medical schools to abandon research programs. See Jaffe & Lerner, supra note 54, at 16-17. Walsh and colleagues report "widespread complaints" about patent holders asserting exclusive rights over potential drug targets. Walsh et al., supra note 91, at 310,

312-14 (discussing several important targets that firms have sought to exclude others from using, including targets related to HIV, cancer, and hepatitis C).

[FN102]. See, e.g., Rebecca Eisenberg, Patents and the Progress of Science: Exclusive Rights and Experimental Use, 56 U. Chi. L. Rev. 1017, 1079-84 (1989) (discussing a case where a patent holder sued a competitor to prevent it from making a preferable, synthetic version of the blood clotting compound Factor VIII); see also David P. Hamilton, Silent Treatment How Genentech, Novartis Stifled a Promising Drug, Wall St. J., Apr. 5, 2005, at A1.

[FN103]. Nat'l Insts. of Health, Report of the National Institutes of Health (NIH) Working Group on Research Tools (1998), http:// www.nih.gov/news/researchtools. NIH reports that firms may seek to either block such research outright, or permit it only if accompanied by a grant-back of a nonexclusive, royalty-free license to any improvements or new uses. Id.

[FN104]. Harvard's exclusive license of the transgenic OncoMouse to DuPont is a well-known example. See Sasha Blaug et al., Managing Innovation: University-Industry Partnerships and the Licensing of the Harvard Mouse, 22 Nature Biotechnology 761, 762 (2004); Walsh et al., supra note 91, at 307-08; Victoria Slind-Flor, Can These Mice Be Saved?; Fenwick Lawyers Say That DuPont's Licensing Terms Are Preventing Researchers from Using the Harvard Mouse, IP L. & Bus., Sept. 30, 2004, at 11.

[FN105]. See Malaria Vaccine Initiative at PATH, Malaria Antigen Patent Access Project Background Information 2 (Mar. 2005) (unpublished manuscript, on file with authors).

[FN106]. See Walsh et al., supra note 91, at 324-26.

[FN107]. Id. at 235. The Federal Circuit in Madey v. Duke University reiterated that the common law research exemption applies only to research conducted “for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry,” and further held that the exemption “does not immunize use that is in any way commercial in nature,” even if that research occurs at a nonprofit institution. 307 F.3d 1351, 1362 (Fed. Cir. 2002), cert. denied, 539 U.S. 958 (2003). Congress has created a statutory exemption for research “reasonably related to the development and submission of information” under federal drug regulations. 35 U.S.C. §271(e)(1) (2000). This exemption has been used to aid companies preparing, just prior to patent expiration, to launch generic products. The limits of this exception are currently under review at the Supreme Court. Merck KGaA v. Integra Lifesciences I, Ltd., 331 F.3d 860 (2003), cert. granted, 125 S. Ct. 823 (2005).

[FN108]. See Jon F. Merz et al., Diagnostic Testing Fails the Test, 415 Nature 577 (2002) (discussing a series of actions brought by companies to stop academic labs from using patented diagnostic tests).

[FN109]. Rebecca S. Eisenberg, Patent Swords and Shields, 299 Science 1018 (2003) (“With their large endowments and habits of documenting their activities in scientific publications, universities would make easy targets.”); see also Rai, supra note 96, at 295.

[FN110]. Little is known about how widespread research tool patenting has become outside the United States and other wealthy countries. In the agricultural context, some have argued that concerns about IPRs impeding “research oriented toward food crops for the developing world” are overblown because there are few patent barriers in developing countries. See, e.g., Eran Binenbaum et al., South-North Trade, Intellectual Property Jurisdictions, and Freedom To Operate in Agricultural Research on Staple Crops, 51 Eco. Dev. & Cultural Change 309, 310, 317 (2003). Others have contended that patents on research tools in developing countries may, in fact, have posed barriers to the development and commercializ-

ation of GoldenRice™. See Golden Rice and Trojan Trade Reps: A Case Study in the Public's Mismanagement of Intellectual Property, RAFI Communique, Sept./Oct. 2000, at 1 (finding a significant number of patents in developing countries but concluding that these patents should not have been considered "insurmountable obstacles"), http://www.etcgroup.org/documents/com_goldenrice.pdf.

[FN111]. See Walsh et al., supra note 91, at 328.

[FN112]. Blocking patents arise when a subsequent inventor patents something novel but still within the scope of the original patent. As a result, each party can block the other from making, using, or distributing the follow-on invention. See Donald S. Chisum, 1 Chisum on Patents Glossary (2004). Bargaining breakdowns may be likely in such situations. See Robert Merges, Intellectual Property Rights and Bargaining Breakdown: The Case of Blocking Patents, 62. Tenn. L. Rev. 75, 75 (1994). Many countries provide for compulsory licensing of blocking patents, with no demonstrably negative effects on investment in research. Merges, supra, at 103-05.

[FN113]. See, e.g., Michael Kremer & Rachel Glennerster, Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases (2004); Carlos M. Correa, Public Health and Patent Legislation in Developing Countries, 3 Tul. J. Tech. & Intell. Prop. 1 (2001); Patricia M. Danzon & Adrian Towse, Differential Prices for Pharmaceuticals: Reconciling Access, R&D and Patents, 3 Int'l J. Health Care Fin. & Econ. 183 (2003); Lanjouw, supra note 88; Susan K. Sell, TRIPS and the Access to Medicines Campaign, 20 Wis. Int'l L.J. 481 (2002).

[FN114]. See, e.g., Editorial, The Plagues of Poverty, N.Y. Times, Mar. 19, 2002, at A22 (mentioning the work of the Gates Foundation and Médecins Sans Frontières); Drugs for Neglected Diseases Initiative, at http://www.dndi.org (last visited Mar. 30, 2005); HealthGAP, Health Global Access Project (GAP), at http://www.healthgap.org (last visited Mar. 30, 2005).

[FN115]. Beginning in 2001, the WTO's attention turned to the issue of access leading to the adoption of the Doha Declaration. Doha Declaration, supra note 47; see also World Trade Org., TRIPS and Public Health, at http://www.wto.org/english/tratop_e/trips_e/pharmpatent_e.htm (last visited Mar. 11, 2005). In 2000, the WHO and UNAIDS developed the Accelerating Access Initiative, see UNAIDS & World Health Org., Accelerating Access Initiative 1 (2002), http://www.who.int/hiv/pub/prev_care/en/isbn9241210125.pdf, and in late 2003 launched the 3 x 5 Initiative, see World Health Org., Fact Sheet 274: The 3 x 5 Initiative (Dec. 2003), at http://www.who.int/mediacentre/factsheets/2003/fs274/en.

[FN116]. Over one hundred countries have developed national drug policies. Quick, supra note 61, at 1.

[FN117]. The Consumer Project on Technology has advocated compulsory licensing and recently created a new nonprofit, Essential Inventions, that plans to request compulsory licenses for AIDS drugs in LMI countries. See Essential Inventions, at http://www.essentialinventions.org (last visited Feb. 24, 2005).

[FN118]. See, e.g., Sanjay Kumar, India To Extend Price Controls on Drugs, 329 BMJ 368 (2004); Andrew Quinn, S. Africa Rules Aim To Cut Drug Prices up to 70 Pct, Reuters NewsMedia, Jan. 15, 2004 (discussing price controls in South Africa), http://www.aegis.com/news/re/2004/RE040113.html. Numerous countries have implemented mechanisms to control or influence pharmaceutical prices. See, e.g., Austl. Gov't Dep't of Health & Ageing, About the PBS, at http://www.health.gov.au/pbs/general/aboutus.htm (last modified Dec. 24, 2003) (describing the Australian Pharmaceutical Benefits Scheme); Can., Patented Med. Prices Review Bd., http://www.pmprb-cepmb.gc.ca (last visited May 6, 2005). However, for a variety of reasons, price controls are an "unsatisfactory policy instrument," particularly for developing countries. Robert Weissman, A Long, Strange TRIPS: The Pharmaceutical Industry Drive To Harmonize Global Intellec-

tual Property Rules, and the Remaining WTO Legal Alternatives Available to Third World Countries, 17 U. Pa. J. Int'l Econ. L. 1069, 1115 (1996) (noting that price controls are difficult for governments to administer and may produce sub-optimal reductions in price due to uncertain data); see Outterson, supra note 72, at 239-40 (explaining that price controls fail to take a number of important considerations into account); Jean O. Lanjouw, Patents, Price Controls, and Access to New Drugs: How Policy Affects Global Market Entry 2 (Apr. 19, 2005) (unpublished manuscript prepared for the WHO Comm'n on Intellectual Prop. Rights, on file with authors) (finding that price controls may delay market entry of new drugs in poor countries).

[FN119]. See, e.g., T.N. Srinivasan, The TRIPS Agreement, in The Political Economy of International Trade Law 343 (Daniel L.M. Kennedy & James D. Southwick eds., 2002).

[FN120]. See, e.g., Jean O. Lanjouw, A New Global Patent Regime for Diseases: U.S. and International Legal Issues, 16 Harv. J.L. & Tech. 85 (2002) (discussing Lanjouw's Foreign Filing License proposal).

[FN121]. See, e.g., Carlos M. Correa, Intellectual Property Rights, the WTO and Developing Countries: The TRIPS Agreement and Policy Options (2000) (describing ways in which developing countries can implement TRIPS while still maintaining maximal flexibility and public health benefits).

[FN122]. See TRIPS Agreement, supra note 47, art. 31; Doha Declaration, supra note 47, P5(b) ("Each Member has the right to grant compulsory licenses and the freedom to determine the grounds upon which such licenses are granted.").

[FN123]. See TRIPS Agreement, supra note 47, art. 31.

[FN124]. Doha Declaration, supra note 47, P7. Despite this flexibility, patent protection for pharmaceuticals has already been established in all but a few African LDCs. See Carlos M. Correa, Implications of the Doha Declaration on the TRIPS Agreement and Public Health 38 (World Health Org., EDM Series No. 12, 2002); Phil Thorpe, Study on the Implementation of the TRIPS Agreement by Developing Countries 1 (Comm'n on Intellectual Prop. Rights, Study Paper 7, 2004).

[FN125]. See Fink & Reichenmiller, supra note 48, at 1 tbl.1. The majority of these are developing countries. Congress has approved agreements with Vietnam, Jordan, Singapore, Chile, Morocco, and Australia. The CAFTA Agreement, which includes the Dominican Republic, Costa Rica, El Salvador, Guatemala, Honduras, and Nicaragua, and the agreement with Bahrain have been signed but not yet approved by Congress. Agreements are currently under negotiation with three Andean countries (Columbia, Ecuador, and Peru), Thailand, Panama, the countries of the Southern African Customs Union (South Africa, Namibia, Botswana, Lesotho, and Swaziland), and the group of countries involved in the Free Trade Area of the Americas. Id.

[FN126]. Id. at 2.

[FN127]. Id. Note that the U.S. Trade Representative (USTR) is arguably exceeding its mandate in these negotiations, which requires it to "respect the Declaration of the TRIPS Agreement and Public Health adopted at Doha." Bipartisan Trade Promotion Authority Act of 2002 §2102(b)(4)(C), 19 U.S.C.A. §3802(b)(4)(C) (West 2004).

[FN128]. See Outterson, supra note 72, at 225. The United States withdrew its request for a WTO panel only after substantial international pressure. Id.

[FN129]. See Ravi Nessman, South Africa Fights over AIDS Drugs, Associated Press, Mar. 5, 2001 (recalling threats by the United States following the passage in 1997 of an amendment to permit compulsory licensing in South Africa), ht-

tp://www.aegis.com/news/ap/2001/AP010302.html.

[FN130]. The Special 301 watch list identifies countries that, in the judgment of the USTR, do not provide adequate protection for U.S. intellectual property. See 19 U.S.C. §2241 (2000). Section 301 of the Trade Act authorizes the executive to impose trade sanctions against such states. See id. §§2411, 2414.

[FN131]. E.g., Office of U.S. Trade Representative, 2004 Special 301 Report (2004), http://www.ustr.gov/assets/Document_Library/Reports_ Publications/ 2004/2004_Special_301/asset_upload_file16_5995.pdf; Office of U.S. Trade Representative, 2003 Special 301 Report (2003), http:// www.ustr.gov/assets/Document_Library/Reports_Publications/2003/2003_Special_ 301_Report/asset_upload_file665_6124.pdf; Office of U.S. Trade Representative, 2002 Special 301 Report (2002), http://www.ustr.gov/assets/Document_ Library/Reports_Publications/2002/2002_Special_301_Report/asset_upload_file567_ 6367.pdf; see Drahos with Braithwaite, supra note 47, at 93-95 (discussing the role intellectual-property-based industries play in the 301 process).

[FN132]. See, e.g., Zita Lazzarini, Making Access to Pharmaceuticals A Reality: Legal Options Under TRIPS and the Case of Brazil, 6 Yale Hum. Rts. & Dev. L.J. 103, 132 (2003); Nessman, supra note 129.

[FN133]. See Duncan Matthews, WTO Decision on Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health: A Solution to the Access to Essential Medicines Problem?, 7 J. Int'l Econ. L. 73, 86-89, 93 (2004) (describing the United Statesand European Union positions during recent WTO negotiations over countries' ability to export under a compulsory license).

[FN134]. Brazil has repeatedly used the credible threat of compulsory licensing to effectively obtain discounts. See Brazil's National STD/AIDS Programme Announces Largest Drug Price Reduction Deals in Five Years, Kaiser Daily HIV/AIDS Rep., Jan. 20, 2004, http://www.kaisernetwork.org/daily_ reports/rep_index.cfm?hint=1&DR_ID=21751.

[FN135]. See World Bank, PPP GDP 2003, at http:// www.worldbank.org/data/databytopic/GDP_PPP.pdf; World Facts Index, History of Brazil, at http://worldfacts.us/Brazil-history.htm (last visited Feb. 26, 2005).

[FN136]. See, e.g., Cipla Gets Malaysian Nod for AIDS Drugs, Bus. Standard (India), Feb. 25, 2004 (reporting Malaysia's recent compulsory license); Martin Khor, Patents vs. Access to Medicines at AIDS Conference, Daily News (Sri Lanka), Aug. 10, 2004 (reporting Mozambique's recent compulsory license), http://dailynews.lk/2004/08/10/fea11.html.

[FN137]. This may be particularly true where such individuals are ill with a disease as stigmatized as HIV/AIDS.

[FN138]. See, e.g., Sara Davis, Opinion, Hold Beijing To Account for Its AIDS Coverup Before the 2008 Olympics, Int'l Herald Trib., Aug. 25, 2004, at 8; Diddier Fassin & Helen Schneider, The Politics of AIDS in South Africa: Beyond the Controversies, 326 BMJ 495 (2003); Michael Specter, India's Plague, New Yorker, Dec. 17, 2001, at 74. There has been some progress on this front for HIV/AIDS. See, e.g., Lawrence K. Altman, South Africa Says It Will Fight AIDS with a Drug Plan, N.Y. Times, Aug. 9, 2003, at A1.

[FN139]. See Sisule F. Musungu et al., Utilizing TRIPS Flexibilities for Public Health Protection Through South-South Regional Frameworks 24-25 (2004).

[FN140]. See TRIPS Agreement, supra note 47, art. 31(a) (requiring licenses to be decided on the basis of their individual merits). The requirement that in most instances the applicant first make “reasonable” efforts to obtain a license, see id. art. 31(b), can also generate substantial delay if strict parameters for reasonableness are not imposed. Finally, countries

must afford right holders "adequate remuneration," id. art. 31(h), and a form of "judicial review or other independent review." Id. art. 31(i). Establishing procedures to meet these requirements can be burdensome for countries with limited resources.

[FN141]. That is because TRIPS requires that any use without the authorization of the patent holder "be authorized predominantly for the supply of the domestic market of the Member authorizing such use." Id. art. 31(f). This provision has been the subject of intense focus recently, because it could prevent countries without the ability to produce medicines domestically from being able to purchase generics from a country that can. At Doha, the Ministerial agreed to address the issue, and after several years of negotiation, a temporary solution was adopted just prior to the Cancún meeting in 2003. See World Trade Org., General Council, Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health, WT/L/540 (Sept. 1, 2003) [hereinafter WTO, Paragraph 6]. The decision provides that, under limited circumstances, and subject to strict and potentially onerous reporting requirements, countries are free to export generic products for the sole benefits of countries lacking manufacturing capacity. The fix has been heavily criticized, see Elizabeth Becker, Cheaper Medicines for the World's Poor; Trade Rules Altered on Patented Drugs, Int'l Herald Trib., Sept. 2, 2003, at 1, but there is little indication that countries are willing to reopen their acrimonious negotiations. For an in-depth discussion of these issues, see Abbott, supra note 76.

[FN142]. See Hollis, supra note 58, at 18 (proposing a prize system that sets awards according to the number of "disability adjusted life-years"--a common measurement of morbidity and mortality--that a product avoids).

[FN143]. See Tim Hubbard & James Love, A New Trade Framework for Global Healthcare R&D, 2 PLoS Biology 147, 148 (2004), available at http:// biology.plosjournals.org/archive/1545-7885/2/2/pdf/10.1371_ journal.pbio.0020052-S.pdf; Letter from James Love et al. to the WHO Executive Board and the WHO Commission on Intellectual Property, Innovation, and Health (CIPIH) (Feb. 24, 2005) (copy on file with authors) (requesting that the WHO evaluate a proposal for a new global medical R&D treaty). Alternatively, others have suggested that countries (or international agencies or foundation) should fund such research through "pull programs," such as advanced purchase commitments. See, e.g., Kremer, supra note 58, at 82.

[FN144]. Richard A. Epstein, Steady the Course: Property Rights in Genetic Material, in Perspectives on Properties of The Human Genome Project 153, 188-193 (F. Scott Kieff ed., 2003), available at http:// www.wulaw.wustl.edu/Academics/Faculty/Bios/Kieff/HGPIP/Final/GEN_50_CH8.pdf.

[FN145]. For example, the American Intellectual Property Law Association (AIPLA) recently endorsed legislation to establish a statutory research exemption for efforts to understand and evaluate the validity of the patent, to find other methods of making or using the patented subject matter, or to find substitutes for the patented subject matter. Am. Intellectual Prop. Law Ass'n, AIPLA Response to the National Academies Report Entitled "A Patent System for the 21st Century" 25-26 (2004), http:// www.aipla.org/Content/ContentGroups/Issues_and_Advocacy/Comments2/Patent_and_ Trademark_Office/2004/NAS092304.pdf. The American Academy of Arts and Sciences has also convened a working group to consider options for a domestic and international research exemption. See Science & Intellectual Prop. in the Public Interest, Research Exemption Working Group, at http:// sippi.aaas.org/rschexemption.shtml (last visited Mar. 5, 2005).

[FN146]. Bayh-Dole University and Small Business Patent Procedures Act, Pub. L. No. 96-517 §6(a), 1980 U.S.C.C.A.N. (94 Stat.) 3015, 3018-29 (1980) (codified at 35 U.S.C. §§200-212 (2000)). The goals of the Act are to, inter alia, "promote the utilization of inventions arising from federally supported research," "promote the commercialization and public availability of inventions," and "ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inven-

tions." Id. §200.

[FN147]. Arti K. Rai & Rebecca S. Eisenberg, Bayh-Dole Reform and the Progress of Biomedicine, 66 Law & Contemp. Probs. 289, 291 (2003).

[FN148]. See Sonny Bono Copyright Term Extension Act, Pub. L. No. 105-298, 112 Stat. 2827 (1998) (describing lengthening of the copyright term codified at 17 U.S.C. §§108, 203, 301-304); supra note 44 (describing expansion of patentable subject matter); supra note 46 (describing regulatory exclusivity in the United States and internationally).

[FN149]. Some have proposed, for example, that the market- and patent-based pharmaceutical sector proactively change its licensing practices or establish discounts and donation programs to address access concerns. See Attaran, supra note 71, at 163. But cf. Michael A. Friedman, Henk den Besten & Amir Attaran, Out-Licensing: A Practical Approach for Improvement of Access to Medicines in Poor Countries, 361 Lancet 341, 341 (2003) (admitting that "donations or discounts offer only limited, often imperfect, solutions").

[FN150]. See, e.g., 't Hoen, supra note 81, at 294 ("[U]ntil January 2003, ... one pharmaceutical company was charging $2000 a year more in Guatemala than in Switzerland for its AIDS drug. Only after months of public pressure did the price of the drug come down in Guatemala." (citing Roche Cuts Price of AIDS Drug to Nations, Associated Press (Feb. 13, 2003); Drug Company Cuts AIDS Drug Prices in S. Africa, supra note 27. But cf. Boelaert et al., supra note 73, at 840 ("This impressive discount ... was not merely due to public outcry, but mostly as a response to competition by generic drugs.").

[FN151]. Gellman, supra note 23. For example, Pfizer refused to join at the inception of the program, insisting that the U.S. prices of Pfizer's medicines were "good value" and worrying that any discussion of differential pricing would threaten its "'core markets."' Id. (recounting an anonymous source's account of statements made by Pfizer's Senior Vice President Ian C. Read). Some participating companies wanted beneficiary countries to explicitly renounce any use of compulsory licensing or parallel importing in exchange for the price concessions. Eight months after the initiative was announced with great fanfare, four of the five companies still refused to reveal the discounts being offered. Discounts were offered on a country-by-country basis and were only made available to the public sector, which in most countries was not providing treatment. A U.N. official who attempted to obtain the same discounted prices for large private sector firms that wanted to provide ARVs to their employees-- a plan which could have financed treatment for one million patients in five years--recounts the pharmaceutical companies' response: "'They laughed at us."' Id.

[FN152]. For example, although BMS asserted it was selling stavudine below cost in Africa, generic companies have been able to undercut its prices by almost seventy percent. See Meldrum, supra note 29. Similarly, the latest summary of best available worldwide prices for ARVs shows that generics are cheaper than proprietary products for seventeen out of the twenty formulations for which there are both generic and proprietary suppliers. MSF, Untangling the Web, supra note 6, at 9-11 tbl.1a.

[FN153]. MSF, Untangling the Web, supra note 6, at 15-19 tbl.2 (reporting diverse restrictions according to geography and the purchasing entity). Note also that discounts on some second-line therapies are still far from adequate, threatening a looming fiscal crisis in developing country ARV programs as first-line drugs fail and need replacement. See Médecins Sans Frontières, A Guide to the Post-2005 World: TRIPS, R&D, and Access to Medicines (Feb. 25, 2005) (showing that second-line therapies currently cost twenty-six times the amount that first-line therapies cost), at http://www.msf.org/countries/page.cfm?articleid=88694E5B-0FED-434A-A21EDA1006002653.

[FN154]. See Oxfam Int'l, Save the Children & VSO, Beyond Philanthropy: The Pharmaceutical Industry, Corporate So-

cial Responsibility, and the Developing World (2002); Smith, supra note 70 (finding price discounts less effective than generic competition); 't Hoen, supra note 81, at 294 (complaining that ad hoc execution of differential pricing schemes and donation programs has resulted in “efforts [that] have been neither systematic nor sufficient”); Letter from Eugene Schiff, Caribbean Coordinator, Agua Buena Human Rights Association et al., to Mr. Andy Schmeltz & Ms. Konji Sebati, HIV Program, Pfizer (Sept. 17, 2004) (on file with authors) (enumerating the flaws with Pfizer's fluconazole donation program in the Dominican Republic).

[FN155]. See, e.g., Letter from Cipla to the South African Registrar of Patents (Mar. 7, 2001) (requesting a compulsory license on several AIDS medicines for the South African market and noting that their requests for voluntary licenses had been rebuffed), available at http:// www.cptech.org/ip/health/sa/ciplanetsh03072001.html.

[FN156]. See, e.g., Aspen Pharmacare Press Release, supra note 28.

[FN157]. GlaxoSmithKline and Boehrenger Ingelheim refused to extend their licenses to the private sector until 2003, when they were faced with an impending judgment by the South African Competition Commission in a suit charging them with unfair trade practices, including excess pricing of their antiretroviral medicines, and seeking a compulsory license to produce the drugs. Reducing the Price of Antiretroviral Medicines, TAC Newsletter (Treatment Action Campaign, S. Afr.), Oct. 27, 2003, http:// www.tac.org.za/newsletter/2003/ns28_10_2003.htm. To avoid setting this precedent and becoming subject to compulsory licenses, the companies settled, and as a result have since entered into additional licenses that permit private sector sales. See, e.g., GlaxoSmithKline Issues Voluntary License for Lamivudine, Zidovudine to South African Generic Drug Company, Kaiser Daily HIV/AIDS Rep., July 1, 2004, at http://www.kaisernetwork.org/daily_reports/rep_ index.cfm?hint=1&DR_ID=24507. Merck followed suit by granting a voluntary license to its AIDS drug to the main South African generic manufacturer. See Press Release, Merck & Co., Inc., Grants License for HIV/AIDS Drug Efavirenz to South African Company, Thembalami Pharmaceuticals (July 13, 2004), http:// www.pressmethod.com/releasestorage/5003645.htm. There has also been one such license in Kenya. See Press Release, GlaxoSmithKline, GlaxoSmithKline Grants a Fourth Voluntary License for the Manufacture and Sale of HIV/AIDS Medicines in Africa (Sept. 22, 2004), http://www.gsk.com//press_archive/press2004/press_ 09222004.pdf.

[FN158]. E-mail from Ellen 't Hoen, Acting Director, Campaign for Access to Essential Medicines, Médecins Sans Frontières, to Amy Kapczynski (Jan. 20, 2005).

[FN159]. For example, a search of the Tanzanian Food and Drugs Authority website, http://www.tfda.or.tz, reveals that several generic forms of AZT (zidovudine) are registered in the country, despite the fact that AZT is patented there, see Tanzanian Patent No. 2429 (issued Sept. 30, 1991). The Clinton Foundation HIV/AIDS Initiative has also publicly stated that it intended to supply generics, including AZT, to the Tanzanian market, see Lawrence K. Altman, Clinton Group Gets Discount for AIDS Drugs, N.Y. Times, Oct. 24, 2003, at A8, but has not announced an intention to obtain a license there. Despite this, there have been no reports of infringement actions.

[FN160]. In 2000, GlaxoSmithKline sent cease-and-desist letters to Cipla regarding the generic company's activities in Uganda and in Ghana. See Gellman, supra note 23 (noting that Glaxo sent Cipla a cease-and-desist letter in Uganda in November 2000); Mark Schoofs, Glaxo Enters Fight in Ghana on AIDS Drug, Wall St. J., Dec. 1, 2000, at A3 (reporting that Glaxo had issued a cease-and-desist letter to Cipla, causing it to stop importing ARVs, and, remarkably, that Glaxo appeared not to hold the cited patents in Ghana).

[FN161]. Recently, for example, the Swiss pharmaceutical company Novartis obtained exclusive marketing rights (EMR) in India for its drug Gleevec, which treats chronic myeloid leukemia and has no therapeutic equivalents. Most of the generic companies producing Gleevec before the EMR issued left the market, and Novartis brought suit to enjoin the others

from selling the drug. The company charges more than ten times the generic price. See Prati Jatania, In Search of the Sugar-Coating: The New Product Patents Regime Will Decide the Future of Hundreds of Leukemia Patients, Indian Express, Dec. 19, 2004. As a result, the Indian government is apparently considering withdrawing the EMR. See Priya Ranjan Dash, Govt Puts Novartis Cancer Drug on Notice, Times India, Feb. 15, 2005, http://timesofindia.indiatimes.com/articleshow/1022035.cms.

[FN162]. See Robert P. Merges, A New Dynamism in the Public Domain, 71 U. Chi. L. Rev. 183, 188 (2004).

[FN163]. Several companies that supply reagents and research equipment are organizing against the AIPLA-proposed statutory research exemption discussed supra note 145. See Memorandum from Janet Lynch Lambert of Invitrogen & Paul Grossman of Applied BioSystems to Interested Members of the Life Science Community (Mar. 8, 2005) (on file with authors).

[FN164]. Commentators anticipate that the access gap will grow wider in years to come, citing factors including the continued growth and influence of multinational pharmaceutical companies and the strengthening of IP protections through international agreements. See, e.g., Oxfam Int'l, Undermining Access to Medicines: Comparison of Five US FTAs (2004), http:// www.oxfamamerica.org/pdfs/fta_comparison.pdf; Mary Crewe, Spectacular Failure--A View from the Epicenter, 4 Yale J. Health Pol'y L. & Ethics 157, 160 (2004).

[FN165]. See Benkler, supra note 39, at 372.

[FN166]. See Weber, supra note 38, at 5-6.

[FN167]. See The GNU General Public License (GPL), at http:// www.opensource.org/licenses/gpl-license.php (last visited Mar. 9, 2005). Although there are now many kinds of open source software licenses, the GPL is by far the most commonly used. See Lerner & Tirole, supra note 38, at 23 tbl.1.

[FN168]. Lerner & Tirole, supra note 38, at 4.

[FN169]. Weber, supra note 38, at 46-47.

[FN170]. Id. at 182.

[FN171]. See Benkler, supra note 39, at 379-80.

[FN172]. Creative Commons, About Us, at http:// creativecommons.org/about/history (last visited Apr. 28, 2005).

[FN173]. Creative Commons, Licenses Explained, at http:// creativecommons.org/about/licenses (last visited Apr. 28, 2005).

[FN174]. Id.

[FN175]. Id.

[FN176]. Pub. Library of Sci., About PLoS, at http:// www.publiclibraryofscience.org/about/index.html (last visited Apr. 20, 2005).

[FN177]. Id.

[FN178]. See Policy on Enhancing Public Access to Archived Publications Resulting from NIH-Funded Research, 70 Fed. Reg. 6891, 6899-900 (Feb. 9, 2005).

[FN179]. Id.

[FN180]. See John Sulston, Intellectual Property and the Human Genome, in Global Intellectual Property Rights: Knowledge, Access and Development 61, 64 (Peter Drahos & Ruth Mayne eds., 2002).

[FN181]. See Ewan Birney et al., An Overview of Ensembl, 14 Genome Res. 925, 925 (2004); Ensembl Genome Browser, at http://www.ensembl.org (last visited Apr. 20, 2005).

[FN182]. See Int'l HapMap Project, at http://www.hapmap.org (last updated Mar. 3, 2005).

[FN183]. See Int'l HapMap Project, Registration for Access to the HapMap Project Genotype Database, at http://www.hapmap.org/cgi-perl/registration (last updated Mar. 3, 2005). The license was "not intended to block the ability of users to file for intellectual property protection on specific haplotypes for which they have identified associated phenotypes, such as disease susceptibility, drug responsiveness, or other biological utility," but merely to preserve public access to HapMap data. Id. This requirement likely stems from the conflict between the HGP and Celera, a private company that made use of HGP data but kept its own secret, and sought to patent resulting gene sequences. See Sulston, supra note 180, at 64. This restriction on so-called "parasitic patenting" has since been dropped, for two reasons. The HapMap consortium felt that the map and surrounding science has advanced to the stage where any haplotypes derived from their released data would be obvious and thus unpatentable. In addition, the leadership was concerned that the license prevented their data from being included in other public genome databases. See Press Release, National Institutes of Health, International HapMap Consortium Widens Data Access (Dec. 10, 2004), http://www.nih.gov/news/pr/dec2004/nhgri-10.htm.

[FN184]. See Biological Innovation for Open Society (BIOS), at http:// www.bios.net (last updated Apr. 17, 2005).

[FN185]. CAMBIA CEO Richard Jefferson describes the motivation behind the effort: "'So much of what we want to do is all tied up in somebody's intellectual property .... It's a complete sclerotic mess, where nobody has any freedom of movement. Everything that open source has been fighting in software is exactly where we find ourselves now with biotechnology."' Thomas Goetz, Open Source Everywhere, Wired, Nov. 2003, http:// www.wired.com/wired/archive/11.11/opensource_pr.html.

[FN186]. See Andrew Pollack, Open-Source Practices for Biotechnology, N.Y. Times, Feb. 10, 2005, at C8 (quoting Gary Toenniessen of the Rockefeller Foundation).

[FN187]. The CAMBIA BIOS License Agreement Version 1.1, at http:// www.bios.net/daisy/license/210 (last updated Feb. 8, 2005).

[FN188]. In the context of universities, the answer is largely a combination of government grants, tuition, and philanthropic giving. See infra notes 212-13 and accompanying text. Strategies that abstain from enforcing IPR exclusivity therefore have little effect on provisioning by the academic sector .

[FN189]. Luis A. Salicrup et al., An Innovative Program To Move Biomedical Health Technologies from the Laboratory to Worldwide Application, 12 IP Strategy Today 1, 7 (2005). Because these provisions are new, none have been enforced yet. Id.

[FN190]. Memorandum of Understanding between the Government of Samoa and the Regents of the University of California, Berkeley for Disposition of Future Revenue from Licensing of Prostratin Gene Sequences, an Anti-Viral Molecule §VI (Aug. 13, 2004) (on file with authors); see also Press Release, University of California, Berkeley, Landmark Agreement Between Samoa and UC Berkeley Could Help Search for AIDS Cure (Sept. 29, 2004), http://www.berkeley.edu/news/media/releases/2004/09/29_samoa.shtml.

[FN191]. See Prospective Grant of Partially-Exclusive Licenses: Human-Bovine Reassortant Rotavirus Vaccine, 69 Fed. Reg. 57,335 (Sept. 24, 2004). Two Indian companies were offered co-exclusive licenses, a Brazilian company was offered an exclusive license, and Chinese companies were offered nonexclusive licenses. Id.; see also Salicrup et al., supra note 189, at 9 (noting that "[t]he degree of exclusivity was determined by the needs of prospective licensees in each country"). Note also that the licensed territories exclude the United States, Canada, and Europe. See Prospective Grant of Partially-Exclusive Licenses: Human-Bovine Reassortant Rotavirus Vaccine, 69 Fed. Reg. at 57,335.

[FN192]. For example, those working on global diseases that are found in rich countries are likely to be able to attract more interest from private industry partners. See Drugs for Neglected Diseases Initiative, Questions and Answers, http://www.dndi.org/cms/public_html/insidearticleListing.asp?CategoryId=160&ArticleId=309&TemplateId=2#mostnegdiseases (last visited Apr. 28, 2005) (noting that initiatives targeting HIV/AIDS, malaria, and TB "have relied heavily on market-based incentive mechanisms, including public-private partnerships," and that these mechanisms are less likely to be effective for the most neglected diseases).

[FN193]. See Barton, supra note 51, at 151 ("These efforts involve public or donor funds and often work in cooperation with the private sector.").

[FN194]. This approach is taken by the TB Alliance and IAVI. See Ctr. for Mgmt. of IP in Health R&D, MIHR: Handbook of Best Practices for Management of Intellectual Property in Health Research and Development app.D, at 193-94, 198 (Richard Mahoney ed., 2003). The TB Alliance gives no details about the precise conditions it negotiates. IAVI's policy is to negotiate reasonable pricing requirements for sales to the public sector in LMI countries as defined by the World Bank. Id. at 198.

[FN195]. This is the approach taken by the International Vaccine Institute. See id. at 194-95.

[FN196]. Id. at 193.

[FN197]. Id. at 194.

[FN198]. Press Release, Yale University, Institute for OneWorld Health Licenses Potent Therapy from Yale and University of Washington To Treat Chagas, One of the Largest Paristic Diseases in the World (July 8, 2003), http://www.yale.edu/opa/newsr/03-07-08-01.all.html.

[FN199]. Id.

[FN200]. Associated Press, UC Santa Barbara Patent Gift To Aid Parasite Fight, San Jose Mercury News, Feb. 24, 2004, at http:// www.mercurynews.com/mld/mercurynews/news/local/8031289.htm (free subscription site).

[FN201]. See, e.g., University of Chicago, Guidelines for Grant and Contract Management, at http://researchadmin.uchicago.edu/guidelines/300/312.shtml (last visited Apr. 10, 2005) (noting that the university will "make every effort to reserve rights to the [exclusively] licensed material to the University and other non-profit institutions").

[FN202]. See, e.g., Best Practices for the Licensing of Genomic Inventions, 69 Fed. Reg. 67,747, 67,748 (proposed Nov. 19, 2004) (noting that the Public Health Service "believes that it is important for funding recipients and the intramural technology transfer community to reserve in their license agreements the right to use the licensed technologies for their own research and educational uses, and to allow other non-profit institutions to do the same"); see also NIH Office of Technology Transfer, Model PHS Patent License Agreement--Exclusive, at http://ott.od.nih.gov/pdfs/Exclusiv.pdf (last visited May 5, 2005).

[FN203]. See, e.g., Baylor Coll. of Med., Exclusive License Agreement (Therapeutic) §2.2, at http://research.bcm.tmc.edu/BLG/bcmt-models.html (last visited Apr. 10, 2005); Univ. of Iowa, Model License Agreement §2.3(b), at http://research.uiowa.edu/techtransfer/forms/model.pdf (last visited Apr. 10, 2005).

[FN204]. Stanford Univ., Exclusive Agreement 2, §3.4, http:// otl.stanford.edu/industry/resources/exclusive.pdf (last visited Mar. 28, 2005) ("Stanford retains the right, on behalf of itself and all other nonprofit academic research institutions, to practice the Licensed Patent and use Technology for any purpose, including sponsored research and collaborations.").

[FN205]. See Wisconsin Alumni Research Found., Standard Non-Exclusive License Agreement 1, §2B(i), at http:// www.warf.ws/uploads/media/20031002132027680_Std_non_exclusive_license_ agrmt.pdf (last visited Apr. 28, 2005).

[FN206]. One additional example that bears mention is a call for an open source, sharing-based model to promote the development of medicines for neglected diseases. See Stephen M. Maurer et al., Finding Cures for Tropical Diseases: Is Open Source an Answer?, 1 PLoS Med. 183, 183 (2004). Called the "Tropical Diseases Initiative," it aims to capitalize on the convergence between computation and computational biology by creating a "decentralized, Web-based, community-wide effort" where public and private sector scientists would work together to enhance the research base for specific neglected diseases (for example, by searching for protein targets or molecules that would work against known targets). Id. at 183-84. Central to the initative's efforts would be a commitment to some type of open licensing scheme. Id. at 183.

[FN207]. Pub. Intellectual Prop. Res. for Agric., Background, at http:// www.pipra.org/background.htm (last visited Mar. 12, 2005).

[FN208]. Pub. Intellectual Prop. Res. for Agric., Draft Definition of Humanitarian Use (2005) (on file with authors).

[FN209]. See Pub. Intellectual Prop. Res. for Agric., Activities, at http:// www.pipra.org/activities.htm (last visited Mar. 28, 2005).

[FN210]. E.g., Nat'l Sci. Bd., Science and Engineering Indicators 2004, at 5-5, 5-8; cf. Francis Narin et al., The Increasing Linkage Between U.S. Technology and Public Science, 26 Res. Pol'y 317, 328 (1997) (showing that 73.3% of all the papers cited in U.S. industry patents from 1993-94 were from public science).

[FN211]. David C. Mowery et al., The Growth of Patenting and Licensing by U.S. Universities: An Assessment of the Effects of the Bayh-Dole Act of 1980, 30 Res. Pol'y 99, 101 (2001).

[FN212]. In 2001, the federal government provided fifty-nine percent of all academic research funds. See Nat'l Sci. Bd., supra note 210, at 5-5.

[FN213]. Industry funded 6.8% of such research in 2001, up from only 2.8% in 1972. Id. Academic institutions themselves accounted for another 20% in 2001, nearly doubling their share of total R&D support since the early 1970s. Id.

[FN214]. See, e.g., Wesley M. Cohen et al., Links and Impacts: The Influence of Public Research on Industrial R&D, 48 Mgmt. Sci. 1 (2002) (describing the traditional view of public research); Jerry G. Thursby et al., Objectives, Characteristics and Outcomes of University Licensing: A Survey of Major U.S. Universities, 26 J. Tech. Transfer 59 (2001).

[FN215]. See Mowery et al., supra note 211, at 101.

[FN216]. Id.; see also Cohen et al., supra note 214, at 1-2 (rejecting the "linear model" that casts universities mainly as incubators of basic research and concluding from a survey of R&D managers from many industries, including the pharmaceutical industry, that government and university research is "used at least as frequently to address existing problems and needs as to suggest new research efforts").

[FN217]. See, e.g., Cohen et al., supra note 214, at 1, 8-10 (concluding that university and government research labs have a "substantial impact on industrial R&D in a few industries, particularly pharmaceuticals"); Alvin K. Klevorick et al., On the Sources and Significance of Interindustry Differences in Technological Opportunities, 24 Res. Pol'y 185, 197 (1995) (noting that "almost all the industries that value the contribution of the biological sciences generically ... also value university-based contributions in that field"); see also Adam B. Jaffe, Real Effects of Academic Research, 79 Am. Econ. Rev. 957, 967 (1989) (discussing geographic spillover effects from universities to industry, which are "statistically strongest in [d]rugs").

[FN218]. See Edwin Mansfield, Academic Research and Industrial Innovation, 20 Res. Pol'y 1, 2-3 & tbl.1 (1991).

[FN219]. See Iain Cockburn & Rebecca Henderson, Public-Private Interaction and the Productivity of Pharmaceutical Research 5 (Nat'l Bureau Econ. Research, Working Paper No. 6018, 1997) (noting that without the contribution of universities and other public sector research institutions approximately sixty percent of thirty-two innovative medicines studied "'would not have been discovered or would have had their discoveries markedly delayed"' (quoting Robert A. Maxwell & Shohreh B. Eckhardt, Drug Discovery: A Case Book and Analysis (1990)); see also Senate Joint Economic Comm., The Benefits of Medical Research and the Role of the NIH 27 (2000) (reporting that public research funding was instrumental in developing fifteen of the twenty-one drugs considered by experts to have had the highest therapeutic impact on society).

[FN220]. See Daniel J. Kevles, Principles, Property Rights, and Profits: Historical Reflections on University/Industry Tensions, 8 Accountability Res. 293, 293 (2001).

[FN221]. Nat'l Sci. Bd., supra note 210, at 5-6; see Mowrey et al., supra note 211, at 104 tbl.1. The rate of increase in the number of utility patents issued to universities is much faster than the overall rate of growth of patenting during the period; during the same time period the number of utility patents issued to U.S. applicants by the PTO did not even double. Compare Mowery et al., supra note 211, at 104 tbl.1 (citing number of utility patents issued to universities from 1969-97), with U.S. Patent & Trademark Office, U.S. Patent Statistics, Calendar Years 1963-2003, http://www.uspto.gov/web/offices/ac/Fido/oeip/taf/us_stat.pdf. Moreover, this growth in university patenting far outpaced the growth in university R&D spending. From 1975 to 1990, "universities increased their patenting per R&D dollar during a period in which overall patenting per R&D dollar was declining." Mowery et al., supra note 211, at 104.

[FN222]. Compare Ass'n of Univ. Tech. Managers, AUTM Licensing Survey: FY 2002, Survey Summary, at 1 tbl.S-6 (2003) [hereinafter 2002 AUTM Survey] (showing 1603 patents issued to responding universities in 1993), with Ass'n of Univ. Tech. Managers, AUTM Licensing Survey: FY 2003, Interim Report, at 1 (2004) [hereinafter 2003 AUTM Interim Report] (showing 3450 patents issued to responding universities in 2003). Note that AUTM surveys only report data from their membership, which does not include all U.S. universities, and that the membership and number of respondents

have grown over time, meaning that responses between years are not strictly comparable. 2002 AUTM Survey, supra, at 6 tbls.S-1, S-2. The 1993 data included responses from eighty-five percent of the top U.S. research universities by research funding, and the 2002 data included responses from ninety-four percent of the same group. Id. at 6 tbl.S-1.

[FN223]. Compare 2002 AUTM Survey, supra note 222 (showing 2227 licenses and options executed in 1993), with 2003 AUTM Interim Report, supra note 222 (showing 4955 licenses and options executed in 2003).

[FN224]. Rai & Eisenberg, supra note 147, at 292.

[FN225]. Although the number of institutions starting TTOs increased throughout the 1970s, that number grew dramatically in the 1980s in the wake of Bayh-Dole. See 2002 AUTM Survey, supra note 222, at 7 figs.1 & 2.

[FN226]. Typically, university scientists are required to report any potentially important innovation--for example, a new molecular entity with pharmacological significance--to their TTO, which then evaluates the invention to determine whether it has commercial potential. See, e.g., Office of Intellectual Prop., Mich. State Univ., Handling Your Invention (2001) ("Researchers are obligated to report any inventions to the [TTO] ...."), http://www.msu.edu/unit/oip/handling.html; see also Lawrence Berkeley Nat'l Lab., How the Tech Transfer Process Works, http://www.lbl.gov/Tech-Transfer/researchers/how-tt-works.html (last visited Mar. 29, 2005) (describing the invention evaluation process and encouraging researchers to contact the TTO to discuss any research that may have produced an invention).

[FN227]. See Rai & Eisenberg, supra note 147, at 293, 301, 309 (discussing the patenting and exclusive licensing of the University of Wisconsin's stem cell patents); id. at 302 (discussing the patenting and exclusive licensing of an important cell signaling pathway by Harvard, MIT, and the Whitehead Institute for Biomedical Research); supra text accompanying notes 104-05. Professor Rai and Professor Eisenberg note that many university patents cover research tools and that "one recent study of Columbia University's patent portfolio indicates that more than 50% of its licensed patents represent research tools." See Rai & Eisenberg, supra note 147, at 292.

[FN228]. See Rai & Eisenberg, supra note 147, at 294.

[FN229]. Id. at 291.

[FN230]. See Nat'l Insts. of Health, supra note 103.

[FN231]. See supra text accompanying note 203.

[FN232]. See Yale Univ. Ctr. for Interdisciplinary Research on AIDS, Access to Essential Medicines and University Research: Building Best Practices 4 (2003) [hereinafter Workshop Report].

[FN233]. Michigan State University held the IPR. See Eyal Press & Jennifer Washburn, The Kept University, Atl. Monthly, Mar. 2000, at 39.

[FN234]. Princeton University holds the IPR. U.S. Patent No. 5,344,932 (issued Sept. 6, 1994).

[FN235]. University of California at San Diego holds the IPR. U.S. Patent No. 4,943,533 (issued July 24, 1990).

[FN236]. Columbia University holds the IPR. See Dep't of Health & Human Servs., Nat'l Insts. of Health, A Plan To Ensure Taxpayers' Interests Are Protected (2001) [hereinafter DHHS/NIH], http:// www.nih.gov/news/070101wyden.htm.

[FN237]. Yale University holds the IPR. U.S. Patent No. 4,978,655 (issued Dec. 18, 1990).

[FN238]. Emory University holds the IPR. See Emory Univ., Office of Tech. Transfer, Product Pipeline 5 (2004), http://www.ott.emory.edu/shared_ web/technologies/Emory_Pipeline.pdf.

[FN239]. University of Minnesota holds the IPR. See Univ. of Minnesota, Fact Sheet on Glaxo-Wellcome AIDS Discovery Settlement (Oct. 5, 1999), http:// www.umn.edu/urelate/newsservice/newsreleases/99_10glaxofacts.html.

[FN240]. Duke University holds the IPRs. U.S. Patent No. 5,464,933 (issued Nov. 7, 1995); U.S. Patent No. 6,133,418 (issued Oct. 17, 2000).

[FN241]. Columbia University holds the IPR. U.S. Patent No. 4,599,353 (issued July 8, 1986); see also Jeff Gerth & Sheryl Gay Stolberg, Medicine Merchants: Birth of a Blockbuster; Drug Makers Reap Profits on Tax-Backed Research, N.Y. Times, Apr. 23, 2000, at 1-1.

[FN242]. For example, Columbia University's co-transformation patent is used to manufacture biotech drugs and has made the university nearly $100 million annually during the patent's life. See Bernard Wysocki Jr., College Try: Columbia's Pursuit of Patent Riches Angers Companies, Wall St. J., Dec. 21, 2004, at A1. Florida State University also holds a key patent on the process to make the cancer drug Taxol. See DHHS/NIH, supra note 236.

[FN243]. See, e.g., Lawrence Berkeley Nat'l Lab., supra note 226.

[FN244]. See Workshop Report, supra note 232, at 4.

[FN245]. Few LMI countries have online patent databases, making it difficult to obtain reliable information on such patents except by directly asking those who may hold them or by consulting local patent offices.

[FN246]. See Workshop Report, supra note 232, at 4; cf. Rebecca S. Eisenberg, Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research, 82 Va. L. Rev. 1663, 1666 (1996) (“If anyone sees money to be made through patenting a government-sponsored research discovery, chances are it will be patented ... [, but] resource constraints prohibit patenting many discoveries that emerge from government-sponsored research.”).

[FN247]. See Lita Nelsen, The Role of University Technology Transfer Operations in Assuring Access to Medicines and Vaccines in Developing Countries, 3 Yale J. Health Pol'y L. & Ethics 301, 304 (2003).

[FN248]. See, e.g., Office of Cooperative Research, Yale Univ., From Bench to Bedside: 1996-1998, at 5 (1999), available at http:// www.yale.edu/ocr/images/docs/ocr_report_96-98.pdf; Jeannette Colyvas et al., How Do University Inventions Get Into Practice?, 48 Mgmt. Sci. 61, 67 (2002) (finding, in an empirical study of university technology transfer, that “the ability to issue exclusive licenses is most important in the context of embryonic inventions,” such as early-stage potential drug compounds); Nelsen, supra note 247, at 303.

[FN249]. Two-thirds of university licensing agreements are made with “newly formed or existing small companies.” Ass'n of Univ. Tech. Managers, AUTM Licensing Survey: FY 2000, Executive Summary, at 1 (2001) [hereinafter 2000 AUTM Survey]; see 2002 AUTM Survey, supra note 222, at 1.

[FN250]. Cf. Big Trouble for Big Pharma, Economist (London), Dec. 4, 2003.

[FN251]. E.g., Bruce Berman, From Tech Transfer to Joint Ventures--Part I, PatentCafe, Mar. 6, 2002, ht-

tp://2xfr.patentcafe.com/article.asp?id=555; see also Maryann Feldman et al., Equity and the Technology Transfer Strategies of American Research Universities, 48 Mgmt. Sci. 105 (2002) (describing the growth of university equity holdings).

[FN252]. E.g., Indiana Univ. Research & Tech. Corp., Inventors & Creators-- What IURTC Negotiates for in Licensing Agreements, http://iurtc.iu.edu/tt_ marketing-terms.html#diligence (last visited Mar. 31, 2005).

[FN253]. See Workshop Report, supra note 232, at 3; Nelsen, supra note 247, at 305. While it is not clear how often such improvement patents are filed in LMI countries, they sometimes are. For example, in Thailand, BMS obtained a patent on the pill form of ddI combined with an antacid buffer, although the underlying compound was not under patent in Thailand. See Tina Rosenberg, Look at Brazil, N.Y. Times, Jan. 28, 2001, §6 (Magazine), at 26. It also seems that such patents will be frequently sought by companies in important source countries like India. There are reportedly over 7000 pharmaceutical patents in India's “mailbox.” See KG Narendranath, Patent Mailbox Opens, Pfizer Is Top Applicant, Fin. Express (India), Mar. 21, 2005 (noting that the vast majority of the patent applications in India's mailbox belong to foreign filers), at http://www.financialexpress.com/fe_full_story.php?content_id=85782. These applications almost certainly include thousands of patents on combinations, formulations, dosages, and other minor improvements. (According to TRIPS, member countries that did not offer patent protection for pharmaceutical and agricultural chemical patents on the date that the Agreement entered into force had to provide patent holders with a means to file such applications, commonly referred to as a “mailbox.” TRIPS Agreement, supra note 47, art. 60.8(i).)

[FN254]. See, e.g., supra note 46.

[FN255]. See Nannerl O. Keohane, The Mission of the Research University, Daedalus, Fall 1993, at 101, 122 (“Proprietary knowledge ... is in principle antithetical to the openness in sharing knowledge that is at the heart of the university's mission.”); cf. Robert King Merton, The Sociology of Science: Theoretical and Empirical Investigations (1973) (describing the “normative structure of science” and finding that one of the institutional mores is collaboration).

[FN256]. Rai & Eisenberg, supra note 147, at 305.

[FN257]. See, e.g., Eisenberg, supra note 246, at 1710 (discussing universities' view of royalties as a measure of TTO success); Thursby et al., supra note 214, at 65-66 (reporting that surveyed TTOs list generating royalties and license fees as the most important measure of TTO success, followed by the number of licenses or options signed).

[FN258]. See Eisenberg, supra note 246, at 1710, 1714-15.

[FN259]. Both individual TTO directors and their national organization have demonstrated interest in these issues. For example, the Director of MIT's Office of Technology Licensing has authored an article encouraging the technology transfer community to learn about its power to promote access to medicines in developing countries and outlining possible strategies in this area. Nelsen, supra note 247, at 303-04; see Jon Soderstrom, Managing Director Office of Cooperative Research Yale University, The Future of University Technology Transfer: Where Do We Go from Here, Presentation to the Gordon Research Conference on Global Aspects of Technology Transfer (Sept. 21, 2003) (encouraging universities to promote technology transfer to benefit developing countries). In December 2003, the Association of University Technology Managers (AUTM) formed a group to examine global health issues. New AUTM Special Interest Group Announced: Technology Transfer Professionals for Global Health, AUTM Newsletter (Ass'n of Univ. Tech. Managers, Northbrook, Ill.), Nov./Dec. 2003, at 9. The 2003 and 2004 AUTM annual meetings included several global-health-related poster presentations and workshops. See Ass'n of Univ. Tech. Managers, AUTM 2004 Annual Meeting [hereinafter AUTM 2004 Meeting], http://www.autm.net/events/eventFiles/AUTM04FP.pdf; Nelsen, supra note 247, at

303.

[FN260]. Cf. Goldie Blumenstyk, A Contrarian Approach to Technology Transfer, Chron. Higher Educ., Mar. 12, 2004, at 27. But cf. Derek Bok, Universities in the Marketplace: The Commercialization of Higher Education (2003) (lamenting the increasing commercialization of universities).

[FN261]. See, e.g., Office of Tech. Licensing, Stanford Univ., OTL and the Inventor: Roles in Technology Transfer, at http:// otl.stanford.edu/inventors/resources/otlandinvent.html (last updated Aug. 8, 2003) ("OTL is responsible for managing the intellectual property assets of the University for the public good."); Office of Tech. Transfer, Univ. of Cal., University of California Patent Policy, http:// www.ucop.edu/ott/patentpolicy/patentpo.html#pol (Oct. 1, 1997) ("The following University of California Patent Policy is adopted to encourage the practical application of University research for the broad public benefit ...."); Tech. Licensing Office, MIT, Mission Statement, http:// web.mit.edu/tlo/www/mission.html (last visited Mar. 31, 2005) ("[Our] mission ... is to benefit the public by moving results of M.I.T. research into societal use via technology licensing ....").

[FN262]. Donald G. McNeil Jr., Yale Pressed To Help Cut Drug Costs in Africa, N.Y. Times, Mar. 12, 2001, at A3.

[FN263]. Univs. Allied for Essential Meds., at http:// www.essentialmedicine.org (last visited Apr. 1, 2005).

[FN264]. See, e.g., Peter Dreier & Richard Appelbaum, The Campus Anti-Sweatshop Movement, Am. Prospect, Sept.-Oct. 1999, at 71, http:// www.prospect.org/print/V10/46/dreier-p.html.

[FN265]. See, e.g., Peter D. Blumberg, Comment, From "Publish or Perish" to "Profit or Perish": Revenues from University Technology Transfer and the 501(c)(3) Tax Exemption, 145 U. Pa. L. Rev. 89 (1996) (arguing that university income from technology transfer should be subject to the unrelated business income tax to the extent TTO practices stray from universities' educational and scientific mission, such as when TTOs license a technology exclusively). The result in the Madey decision also turned in part on the perception that universities are fundamentally analogous to businesses, although formally they are structured as nonprofits. See Madey v. Duke Univ., 307 F.3d 1351 (Fed. Cir. 2002), cert. denied, 539 U.S. 958 (2003).

[FN266]. Bayh-Dole reserves for the government a nonexclusive, nontransferable, irrevocable, paid-up license to practice federally-funded inventions, 35 U.S.C. §202(c)(4) (2000), and the right to force patentees to license government-funded patented inventions to third parties on reasonable terms to ensure the invention's public availability, id. §203. The government may require compulsory licensing if there is inappropriate delay in achieving practical application of the invention, id. §203(1)(a), which includes making the invention available to the public on reasonable terms, id. §201(f), or if licensing is necessary to alleviate health or safety needs, id. §203(1)(b). The NIH also seems to construe these provisions to apply to patents held in other countries. See generally Letter from Harold Varmus, Director, NIH, to Ralph Nader, James Love, and Robert Weissman (Oct. 19, 1999) (discussing but declining to exercise the federal government's power to license patent rights, including foreign patent rights, to the WHO), available at http://www.cptech.org/ip/health/sa/varmusletteroct19.html.

[FN267]. See Barbara M. McGarey & Annette C. Levey, Patents, Products, and Public Health: An Analysis of the CellPro March-In Petition, 14 Berkeley Tech. L.J. 1095 (1999); Nat'l Insts. of Health, Office of the Director, Opinion in the Case of Norvir (Jul. 29, 2004), available at http:// ott.od.nih.gov/Reports/March-In-Norvir.pdf; Nat'l Insts. of Health, Office of the Director, Opinion in the Case of Xalatan (Sept. 17, 2004), available at http://ott.od.nih.gov/Reports/March-In-Xalatan.pdf. Scholars have criticized the NIH's inaction and recommended substantial reforms to the Bayh-Dole regime. See McGarey & Levey, supra; Rai & Eisenberg, supra note 147, at 303-04, 310-13.

[FN268]. Rai & Eisenberg, supra note 147, at 308.

[FN269]. Id. at 309.

[FN270]. William Brody, President of Johns Hopkins University, has observed, "[t]he dirty secret is that for many universities--perhaps most--they are not breaking even, much less making money on the proposition." William R. Brody, From Minds to Minefields: Negotiating the Demilitarized Zone Between Industry and Academia, Remarks at Biomedical Engineering Lecture Series (Apr. 6, 1999), available at http://www.jhu.edu/~president/speech/biomlec.html; see also Bhaven N. Sampat, The Effects of Bayh-Dole on Technology Transfer and the Academic Enterprise: A Survey of the Empirical Literature 12-13 (2004) (unpublished manuscript, on file with authors), http://www.vannevar.gatech.edu/papers/bdsurvey.pdf.

[FN271]. See 2002 AUTM Survey, supra note 222, at 19 fig.25 (showing the distribution of total licensing income received by U.S. universities in 2002); Sampat, supra note 270, at 11-12 (observing that a small fraction of universities realize significant income from licensing, with the only a few schools owning truly lucrative patents).

[FN272]. See Nelsen, supra note 247, at 302 (giving figures of two percent to four percent) (citing 2002 AUTM Survey, supra note 222)).

[FN273]. See Benkler, supra note 36, at 1110.

[FN274]. See Jerry G. Thursby & Marie C. Thursby, University Licensing Under Bayh-Dole: What Are the Issues and Evidence? 4 (May 2003) (unpublished manuscript, on file with authors) ("For all university technologies, an average royalty rate of 2% is common. For pharmaceuticals the maximum rate one typically encounters for university technologies is 5%; however, the rates are usually closer to 1.5%.").

[FN275]. Michael Merson, Preface to Workshop Report, supra note 232, at v. It should be noted, however, that universities often prize even limited income from technology transfer because these funds can in large part be used for any purpose, as opposed to research grants and even donations, which typically may only be used for predefined purposes. See, e.g., Thomas A. Massaro, Innovation, Technology Transfer, and Patent Policy: The University Contribution, 82 Va. L. Rev. 1729, 1735 (1996). Furthermore, a portion of technology transfer monies flow to inventors (typically thirty to forty percent), see 35 U.S.C. § 202(c)(7)(B) (2000) (mandating revenue sharing under Bayh-Dole); Robert L. Barchi, IP and Technology Transfer from the Academic Perspective 19, http://www7.nationalacademies.org/step/Barchi_ppt.ppt (last visited Mar. 31, 2005); Office of Cooperative Research, Yale Univ., Yale Univ. Patent Policy § 4(d) (Feb. 1998), http://www.yale.edu/ocr/invent_ policies/patents.html, which provides direct incentives for university researchers. But given the highly uncertain returns on research, the expected value of patent royalties is small, and the loss of royalties from LMI country sales particularly insignificant, even to those who value unrestrained funds and personal financial incentives the most.

[FN276]. Cf. Big Trouble for Big Pharma, supra note 250 ("Many big drug firms have begun to license more of their technology and products from outside companies, especially biotechnology start-ups."); Jerry G. Thursby & Marie C. Thursby, Who Is Selling the Ivory Tower? Sources of Growth in University Licensing, 48 Mgmt. Sci. 90, 90 (2002) (noting pharmaceutical companies' "increased business reliance on external R&D").

[FN277]. We expect that successful collective action by universities is likely if the dominant players in the technology transfer field take the lead. More than 3000 institutions received NIH funding in FY 2003; twenty-three of the top twenty-five recipients were universities, and they alone garnered thirty-four percent of the total funding awarded in the

United States. See Office of Extramural Res., Nat'l Insts. of Health, Award Trends, Rankings: All Institutions, FY 2003; By State, FY 2003, at http:// grants.nih.gov/grants/award/awardtr.htm#c (last visited Apr. 5, 2005). Of the 112 medical schools earning NIH funding, the top twenty-five received fifty-six percent of the monies. See Office of Extramural Res., Nat'l Insts. of Health, Award Trends, Rankings: Medical Schools, FY 2003, at http:// grants.nih.gov/grants/award/awardtr.htm#c (last visited Apr. 5, 2005). Successful technology transfer deals are similarly concentrated among a small group of elite universities. See 2002 AUTM Survey, supra note 222, at 20 (showing that less than one percent of active licenses generated more than one million dollars in 2002,

[FN278]. Even if possible, this approach would have disadvantages. Patents can be useful for defensive purposes, for example, because they can give the university a bargaining chip in cross-licensing negotiations. Cf. supra note 41.

[FN279]. There are well-established accounting standards to define marginal cost of manufacture, and the university could reserve for itself the right to audit a licensee's books. This would be necessary because patent-based companies have proven generally unwilling to reveal cost in a transparent fashion. See, e.g., Outterson, supra note 72, at 222, 253 n.255 ("Given the endemic opacity of all PhRMA data on costs, perhaps the best way to calculate marginal cost is through compulsory licensure.... Absent the patent monopoly, generic companies in a competitive environment will certainly price much closer to marginal cost than PhRMA companies."). In addition, it would be relatively easy to monitor whether a company was meeting its deadline for drug registration in particular countries, so long as these deadlines are clearly established. Determining whether a company is meeting all existing market need would be more difficult, possibly requiring an investigation into in-country conditions, but may nonetheless be manageable.

[FN280]. A reasonable pricing effort would presumably be plagued with the same kinds of delays and inefficiencies that have adversely affected existing donation and discount programs.

[FN281]. Universities are, in this regard, differently situated from the single-issue public-private partnerships (PPPs). This fact, and the lack of an articulated alternative, may explain why such PPPs have relied heavily upon reasonable pricing requirements to address access concerns.

[FN282]. Parallel trade is a form of arbitrage that puts pressure on companies that seek to price discriminate. See generally Outterson, supra note 72. While TRIPS allows parallel trade of originator products, many countries (such as the United States) prohibit it--either as a matter of patent exhaustion law or as a result of regulatory barriers. See id. at 209-15.

[FN283]. See id. at 257-60 (discussing two alleged instances of dysfunctional arbitrage and determining that the claims were inappropriate or unsubstantiated); id. at 262 ("As of April 2002, both the European Commission and the pharmaceutical companies acknowledged that pharmaceutical arbitrage from poor countries into the high income was 'still largely theoretical."' (citing DG Trade, European Union, Tiered Pricing for Medicines Exported to Developing Countries, Measures To Prevent Their Re-Importation into the EC Market and Tariffs in Developing Countries §3.3 (EU Working Document, 2002))). For detailed responses to pharmaceutical industry concerns about diversion, see Sanjay Basu, Pharmaceutical Product Diversion: Diverting Attention Away from the Real Problem? (Oxfam Briefing Paper No. 35, forthcoming 2005) (manuscript at 3-4, on file with authors) (reporting that "the scope of product diversion and the difficulty of controlling it have been exaggerated by the pharmaceutical industry," and noting that generic drugs have been produced in India for decades without undermining Western markets).

[FN284]. See WTO, Paragraph 6, supra note 141, §2(b)(ii) (requiring product differentiation); see also Basu, supra note 283 (manuscript at 7-8).

[FN285]. Pharmaceutical companies may be particularly concerned about the effects of differential pricing on their negotiations with high-income markets where prices are set by national regulators. See, e.g., Lanjouw, supra note 118, at 2 (describing international pricing externalities).

[FN286]. "A grant-back clause in a patent license requires the licensee to grant back to the licensor patent rights which the licensee may develop or acquire." 6 Donald S. Chisum, Chisum on Patents §19.04[3][j] (2003). Technically, an EA license would utilize both a grant-back (for newly developed or acquired rights) and a cross-licensing mechanism (for any existing licensee rights that could be used to block production of the end product).

[FN287]. Biologics are referred to by a variety of names--including biologicals, macromolecules, and biopharmaceuticals. For an assessment of the biologic medicines and genomic technologies most likely to be of use in developing countries, see Abdallah S. Daar et al., Top Ten Biotechnologies for Improving Health in Developing Countries, 32 Nature Genetics 229, 229-30 (2002).

[FN288]. Biologics are structurally more complex and difficult to characterize than small molecules. Correspondingly, the manufacturing processes are both more complicated and challenging to reproduce--biologics are typically derived from living cells, rather than synthesized through chemical processes. See Shawn Glidden, The Generic Industry Going Biologic, 20 Biotechnology L. Rep. 172 (2001); Michael Kleinberg & Kristen Wilkinson Mosdell, Current and Future Considerations for the New Classes of Biologicals, 61 Am. J. Health-Sys. Pharmacy 695, 695-97, 701-02 (2004) (including a description of the added costs associated with the manufacture of biologics). Although biologic therapies are mostly under patent because they are relatively new, it is estimated that roughly $10 billion worth of these products will be off patent by the end of 2006. Arman H. Nadershahi & Joseph M. Reisman, Generic Biotech Products: Provisions in Patent and Drug Development Law, BioProcess Int'l, Oct. 2003, at 26. Several companies now focus on producing generic biologics, and a number of products have been developed or are in development. See, e.g., Enrico T. Polastro, The Future of Biogenerics: When Will We See Legal Generics of Top Biopharmaceuticals?, Contract Pharma, Oct. 2001 (describing development taking place outside of the principal high-income markets), http:// www.contractpharma.com/Oct013.htm. However, to date, none have been approved in the United States or Europe. In fact, there is not yet an established regulatory framework in the United States to assess and approve generic biologics. See Kleinberg & Mosdell, supra, at 702-03. This regulatory uncertainty stems from the ongoing debate about whether an abbreviated regulatory process--as we have for small molecule generics--is scientifically viable for biologics. See Glidden, supra, at 176-77 (comparing and contrasting the FDA regulatory challenges of biogenerics with two other similar situations); Selena Class, Biogenerics: Waiting for the Green Light, IMS Health, Oct. 28, 2004 (focusing on arguments by makers of biogenerics), at http://www.ims-global.com/insight/news_story/0410/news_story_041027a.htm; FDA Looks at Biogeneric Issue, But Action Unlikely in the Near Term, Specialty Pharmacy News, Nov. 10, 2004 [hereinafter FDA Looks at Biogeneric Issue] (summarizing the debate and describing the European Union's framework for case by case assessment of biosimilar comparability), http:// www.aishealth.com/DrugCosts/specialty/SPNFDABiogeneric.html. The FDA has said that it will issue regulatory guidance this year, but regardless of the outcome, generic biologics may be found in other markets. Mike Faden, Biogenerics Hang at the Starting Gate, Pharm. Bus. Strategies, Mar. 2005, http://www.pbsmag.com/Article.cfm?ID=169; see also FDA Looks at Biogeneric Issue, supra (noting that Australia has approved one biogeneric and that various biogenerics are being sold in Asian and South American markets with relatively lax regulatory systems).

[FN289]. See Nat'l Insts. of Health, supra note 103.

[FN290]. Note that there is no legal or moral reason that universities should limit EA licensing to technologies that come from their pharmacology departments, medical schools, and molecular biology programs. Innovations in fields such as

engineering or agriculture can also have a vital health impact, and we expect that universities will be concerned about LMI country access with regard to any technology that has a health-related--or more broadly, a human welfare--benefit. Our focus, however, is in biomedical technologies. We leave an assessment of the value of EA licensing to these other fields for those who are expert in them. By "health-related," we mean any technology with a demonstrated medical benefit. We are less concerned with EA licensing for so-called "lifestyle" drugs.

[FN291]. Derek Yach et al., The Global Burden of Chronic Diseases, 291 JAMA 2616, 2620 (2004); see also id. (noting that cardiovascular disease accounts for as many deaths in young and middle-aged adults as HIV/AIDS in developing countries).

[FN292]. Id. at 2616. This is of course partly due to the fact that eighty percent of the world's population resides in less developed regions--as do ninety-five percent of new persons added to the world each year. See United Nations Secretariat, The World at Six Billion 3 (1999), ESA/P/WP.154 (citing the U.N. Population Division), http://www.un.org/esa/population/publications/sixbillion/sixbilpart1.pdf.

[FN293]. See Yach et al., supra note 291, at 2616 (noting, for example, that approximately 298 million people in developing countries are expected to suffer from diabetes by 2030).

[FN294]. Id. at 2618 fig.2. Consider also that "[i]n South Africa, infectious diseases account for 28% of years of lives lost, while chronic diseases account for 25%." Id. at 2617.

[FN295]. See Derek Yach & Corinna Hawkes, Towards A WHO Long-Term Strategy for Prevention and Control of Leading Chronic Diseases 11 (2004) (noting that "72% of deaths from all chronic diseases occur in low- and middle-income countries, and death rates are higher among all age groups").

[FN296]. Cf. Wagstaff & Claeson, supra note 63, at 118-19.

[FN297]. The Gini index is the most popular measure of income or resource inequality. A score of 100 on the Gini index would represent absolute inequality (where one person held all the wealth of a society), and a score of zero would represent absolute equality. See Statistics Div.--Advisory Comm. on Indicators, United Nations, at http://unstats.un.org/unsd/indicatorfoc/indsearchpage.asp?cid=87 (last visited Apr. 5, 2005). Many of the middle-income countries that companies might most like to exclude from an EA provision are very high on the Gini index. See United Nations Dev. Programme, Human Development Report 188-91 (2004). For example, Brazil, Mexico, and South Africa all have Gini index values of more than fifty. In Brazil, the richest ten percent consume 46.7% of the country's income, while the richest ten percent in South Africa consumes 46.9% of that country's income. China's Gini index value is 44.7, and Thailand's is 43.2. For comparison purposes, the Gini index value of the United States is 40.8. Id.

[FN298]. See United Nations Dev. Programme, supra note 297, at 147-49. In South Africa, 23.8% of individuals live on less than $2 per day; the comparable numbers for Thailand and China are 32.5% and 46.7% respectively. Id.

[FN299]. See supra notes 65-67 and accompanying text.

[FN300]. Some might object to the inclusion of middle-income countries on the basis that international transfers of wealth should not be directed at countries that have a reasonably high capacity to address access concerns but are failing to do so. However, the only alternative, in this case, is to punish individuals for the inaction of their governments. Furthermore, we are not persuaded that the sharing strategies adopted here are best thought of as "transfers of wealth," since the good being shared is nonrival. Indeed, one might consider that imposing rules requiring limits on market competition

and thus permitting rent-extraction from economies whose demand pull has no positive incentive effect on R&D, by firms located in the rich countries and that orient their research towards demand from rich countries, is a form of regressive tax on access to the international trade system.

[FN301]. See Yach & Hawkes, supra note 295, at 12 (noting that "large middle income, low mortality developing countries"--countries such as China are exactly the ones that companies are most likely to seek to exclude--are particularly heavily affected by chronic diseases).

[FN302]. In order to ensure that the EA structure is self-perpetuating, the license should require that any sublicenses carry the terms of the EA license with them. This is important because the initial license may be with a biotech company, which will sublicense the university technology to a pharmaceutical company only after further development.

[FN303]. This is due to provisions in Article 39.3 of the TRIPS Agreement and the increasingly stringent data exclusivity provisions in free trade agreements. See Scafidi, supra note 46.

[FN304]. National drug regulatory agencies differ widely in the data they require and the processes they follow. Some allow generic companies to rely on the fact that a drug has been registered in another country, or on data that was submitted to regulatory agencies in another country. See Fink & Reichenmiller, supra note 48, at 2-3.

[FN305]. According to a federal district court, for a grant-back license agreement to constitute patent misuse, the licensee generally "must provide specific evidence that the clause actually stifled innovation." Robin Feldman, The Open Source Biotechnology Movement: Is It Patent Misuse?, 6 Minn. J.L. Sci. & Tech. 117, 155 (2004) (discussing Transparent-Wrap Machine Co. v. Stokes & Amith Co., 166 F. Supp. 551 (S.D.N.Y. 1958), and other case law). Thus, exclusive grant-backs may raise concerns, as may agreements that cover products invented using a research tool rather than incorporating a patented invention, but nonexclusive grant-backs are typically acceptable. Id. at 156-59.

[FN306]. Courts typically use two methods to determine whether a patentee's actions constitute misuse: the antitrust rule of reason and the patent policy inquiry. See id. at 167. An antitrust inquiry focuses on whether the licensing agreement has anticompetitive effects and, if so, whether those effects outweigh the agreement's pro-competitive benefits. A patent policy inquiry examines whether the agreement is consistent with patent policy. Cf. id. at 163-65. Because the EA license promotes competition and ultimately seeks to increase rather than restrict competition, it is difficult to argue that any anticompetitive effects exist, or that those effects could outweigh pro-competitive effects. See id. at 163-65. In contrast, one might argue that the EA license conflicts with patent policy because it reduces incentives to innovate, forcing competition for LMI-country markets and thereby reducing licensee profits. But the limited nature of monopoly rents available from LMI markets suggest instead that an EA clause is highly unlikely to harm the patent-based pharmaceutical industry's incentives to innovate, and that it might stimulate innovation by nonprofit and generic pharmaceutical companies. Cf. id. at 159-63.

[FN307]. Cf. 21 U.S.C. §355(j)(5)(B)(iv) (2000) (authorizing a 180-day period of exclusivity for the first generic to enter the market in the United States).

[FN308]. See United Nations Dev. Programme, Human Development Report 108 (2001) (citing a normal rate of four percent, and providing for adjustments up and down), http://www.undp.org/hdr2001/chapterfive.pdf. Other novel approaches to determining royalty rates merit consideration: in May 2004, Canada passed legislation to give effect to the WTO's August 30th decision, which allows Members with manufacturing capacity to export compulsorily licensed drugs for the benefit of Members without such capacity. See WTO, Paragraph 6, supra note 141. Subsequently, the Department of Industry published a draft implementing regulation for public comment. The draft regulation sets forth a novel formula

for calculating the royalties to be paid by the developing nation licensees to the patentees. Currently, calculations using the formula produce a potential range of royalties from .02% to 3.5%. See Use of Patented Products for International Humanitarian Purposes Regulations: Regulatory Impact Analysis Statement and Draft Regulation, Canada Gazette, Oct. 2, 2004, http:// gazetteducanada.gc.ca/partI/2004/20041002/html/regle9-e.html.

[FN309]. If complexity and inequality within middle-income countries were less of a concern, EA licenses could also seek to implement proposed royalty models that better reflected a country's ability to pay. See, e.g., William Jack & Jean O. Lanjouw, Financing Pharmaceutical Innovation: How Much Should Poor Countries Contribute?, 19 World Bank Econ. Rev. (forthcoming 2005), http://www.georgetown.edu/faculty/wgj/jack-lanjouw-draft.pdf.

[FN310]. See Outterson, supra note 72, at 254.

[FN311]. See, e.g., Ranbaxy Pharmaceuticals Inc., Ranbaxy Pharmaceuticals Announces Nationwide Availability of DipserMox™ (First-Ever Amoxicillin Tablets for Oral Suspension) in Time for the Respiratory Season (Nov. 3, 2003), http://www.ranbaxyusa.com/newsroom/03-11-03.htm.

[FN312]. Of course, separate from the matter of rights provided by the EA license, the generic entrant will have to comply with any regulatory requirements in the LMI country (for example, registration) before it will be able to sell its product.

[FN313]. A secondary assurance might also be built into an EA license in the form, for example, of a statement that the acceptance of the notifier's royalty payment represents a covenant not to sue, guaranteeing additional legal protection from any later claims that the patents and products notified for are not covered by the underlying license. The utility of such a mechanism is doubtful, however, given that the rates involved and value of sales will likely be small. High-income market licensees may choose to reject the royalty in order to preserve their options and increase uncertainty.

[FN314]. For a description of GMP, see WHO, World Medicines Situation, supra note 67, at 98 fig.9.1.

[FN315]. A license could turn on registration with the WHO's Prequalification Project, which provides governments and pharmaceutical manufacturers with information about how to ensure the quality, safety, efficacy, and rational use of pharmaceutical products. The Project focuses on a small number of priority medicines, which are, to date, those related to TB, HIV/AIDS, and malaria. World Health Org., Essential Medicines and Policy Dept. (EDM), Prequalification Project, http://mednet3.who.int/prequal/about.htm (last visited Mar. 15, 2005).

[FN316]. See Glidden, supra note 288, at 178-80 (describing the importance of non-patented trade secrets in the manufacture of biologics); Gil Y. Roth, Biomanufacturing Report, Contract Pharma, June 2003 (describing challenges of producing a protein identical to a branded drug without materials or know-how), http://www.contractpharma.com/June032.htm.

[FN317]. A university could deem a licensee who failed to provide enabling know-how or materials in breach of the original primary license, and use its own powers of persuasion to facilitate the enablement. However, a university may be reluctant to travel this road. Cf. supra text accompanying note 281.

[FN318]. See Press Release, IMS Health, IMS Health Reports 2004 Global Pharmaceutical Sales Grew 7 Percent to $550 Billion (Mar. 9, 2005) ("Biotech products accounted for 27 percent of the active research and development pipeline, and 10 percent of global sales in 2004. IMS expects that over the next five years, innovative products derived from biotechnology will continue to grow in the double digits and represent an increasing share of the overall market."), ht-

tp://www.imshealth.com/ims/portal/front/articleC/0,2777,6599_3665_ 71496463,00.html.

[FN319]. See Pub. Intellectual Prop. Res. for Agric., Draft Definition of Humanitarian Use, supra note 208.

[FN320]. This approach has, in fact, been taken in both the WARF standard licenses and the BIOS initiative. See supra notes 187, 205 and accompanying text. Like the EA approach, ND provisions should not conflict with the patent misuse doctrine. See Feldman, supra note 305.

[FN321]. One such list might be derived from the influential Trouiller study. See Trouiller et al., supra note 81, at 2189. An alternative might include any disease with some set proportion of its burden in developing countries. Cf. Kremer, supra note 58, at 71 tbl.3.

[FN322]. 21 U.S.C. §§360bb(a)(2), 360ee(b)(2) (2000); 21 C.F.R pt.316.1 (2004). The FDA has developed specific criteria for classifying orphan drugs. See FDA, Cumulative List of Orphan Drug Products Designated and or Approved Through 2005 (Apr. 6, 2005), at http:// www.fda.gov/orphan/designat/alldes.rtf. To incentivize development of drugs for rare conditions, companies are rewarded with regulatory-based exclusivity. 21 U.S.C. §360cc. As a result, orphan drugs for serious, chronic diseases with small but steady U.S. patient populations may yield substantial revenues. For example, Genzyme makes several hundred million dollars a year on Ceredase, an expensive orphan drug for Gaucher Disease. See, e.g., James Love, The Other Drug War, Am. Prospect, June 1993, at 121, available at http:// www.prospect.org/web/page.ww?section=root&name=ViewPrint&articleId=5121.

[FN323]. See, FDA, Cumulative List of Orphan Drug Products Designated and or Approved Through 2005, supra note 322.

[FN324]. Id. (including dengue fever, Chagas disease, leishmaniasis, malaria, and TB). The FDA has approved orphan drug status for products intended to treat subsets of disease populations; a drug indicated to treat a particular stage or strain of a disease, or a particular category of patients (for example, AIDS patients with symptomatic HIV infection and CD4 count below 200/mm3), may qualify for orphan drug designation. Id.

[FN325]. One model here could be the agreement between the University of California at Berkeley, OneWorld Health, Amyris Biotechnologies, and the Gates Foundation to secure both research freedom and funding to develop a steady, affordable supply of the antimalarial drug artemisinin. Press Release, University of California at Berkeley, $43 Million Grant from Gates Foundation Brings Together Unique Collaboration for Antimalarial Drug (Dec. 13, 2004), http://www.berkeley.edu/news/media/releases/2004/12/13_gates.shtml.

[FN326]. See Rayasam, supra note 86 (describing an effort at the University of Texas to develop an inexpensive, rapid technology to count CD4 cells, an important component of care for individuals with HIV/AIDS).

[FN327]. The NIH Office of Technology Transfer has begun to adopt this approach, and has licensed or is in the process of licensing technologies to institutions in Mexico, Brazil, India, Chile, Argentina, China, Korea, Egypt, Indonesia, South Africa, and other sub-Saharan African countries. Salicrup et al., supra note 189, at 6.

[FN328]. The NIH has offered exclusive, partially exclusive, and nonexclusive licenses covering both patents and biological materials. See id. at 10 tbl.2.

[FN329]. Id. at 9.

[FN330]. For a model license that aims to integrate the EA and ND provisions in this way, see Model Provisions for an

Equitable Access License, at http:// www.essentialmedicine.org/EAL.pdf. We are grateful to all those who participated in the interdisciplinary working group, based at Yale University and organized by Universities Allied for Essential Medicines, to develop this document.

[FN331]. However, such clauses may be unnecessary or inappropriate when dealing with nonprofits of this sort, whose ethos and mission are already closely aligned with those of universities. Because these nonprofits are generally expert in their particular areas of research, they may be better positioned than universities to determine the best strategy to ensure access for researchers and patients. In the artemisinin deal between Berkeley and OneWorld Health, for example, Berkeley granted OneWorld Health an exclusive right to the University's relevant patent rights. See E-mail from Carol Mimura, Director, Office of Technology Licensing, to Yochai Benkler, Professor of Law, Yale Law School (May 6, 2005) (on file with authors).

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