Ensuring Policy and Laws are Both Effective and Just

Academic Patents and Access to Medicines in Developing Countries

Bhaven N. Sampat, PhD, MPhil

There is a widespread and growing concern that patents hinder access to life-saving drugs in developing countries.

Recent student movements and legislative initiatives emphasize the potential role that research universities in developed countries could have in ameliorating this "access gap." These efforts are based on the assumption that universities own patents on a substantial number of drugs and that patents on these drugs are currently filed in developing countries.

I provide empirical evidence regarding these issues and explore the feasibility and desirability of proposals to change university patenting and licensing practices to promote access to medicines in the developing world. (*Am J Public Health*. 2009;99: 9–17. doi:10.2105/AJPH.2007.128769)

THE PHARMACEUTICAL REVO-lution contributed to dramatic reductions in morbidity and mortality from disease in developed countries during the last century. Today, however, as many as 2 billion people in the world—most of them in developing countries—lack access to life-saving drugs.[1] Righting this imbalance is among the most important challenges in global public health in this century. One source of the access gap in developing countries is a lack of research on specific diseases within developing countries. Both the public and private sectors devote relatively little research to diseases without markets in developed countries. As a result, relatively few new drugs target diseases specific to developing countries.[2] Analysts have also argued that poor health infrastructure, cumbersome drug regulatory procedures, and high tariffs and taxes in developing countries are important obstacles to access.[3] A third potential obstacle—my focus—is pharmaceutical patenting in developing countries, which (by restricting generic competition) can raise the prices of drugs and thus hinder access to medicines.

One proposed solution to this last problem targets a perhaps surprising set of actors: research universities and public sector research institutes in developed countries. One of the main advocates of this approach, Universities Allied for Essential Medicines, a student group with over 40 campus chapters (with the slogan "Our Labs, Our Drugs, Our Responsibility") argues on its Web site:

> Many of the world's most important medicines and public health devices are wholly or partly developed in academic laboratories. Their accessibility to those living in poor nations is profoundly affected by the research, licensing and patenting decisions made by universities. . . . As members of these institutions of higher learning, we believe that universities have an opportunity and a responsibility to improve global access to public health goods—particularly those they have helped develop.[4]

I explore the feasibility and desirability of proposals to use the power of universities—conferred by ownership of key patents—to help reduce drug prices and promote access in developing countries. I provide and discuss new data, university ownership of key patents, and their propensity to file these patents in developing countries. However, before doing so, it is useful to reflect on the broader institutional and historical context for the current proposals. Drug patents allow their owners to exclude others from using or producing the drug until patent expiration (typically 20 years from the date the patent is filed). By excluding generic competition, patents keep prices high. The typical justification for patent protection is that these temporary high prices are needed to create incentives for firms to invest in research and development. In other words, patents involve tradeoffs: although they create incentives to innovate, they can raise prices and reduce access.

Until the mid-1990s, many developing countries did not allow product patents in pharmaceuticals.[5] This generally reflected a conscious policy decision that the benefits from low-cost access to drugs were greater than any potential negative impact that lack of domestic patents would have on the research and development decisions of multinational companies. However, following the World Trade Organization's 1995 Trade-Related Intellectual Property Rights (TRIPs) agreement, all countries were compelled to allow product patents in pharmaceuticals. In the post-TRIPs era, there is widespread concern that, by raising prices, drug patents will reduce access to medicines in developing countries.[6]

University patenting, too, is a relatively recent development.

Throughout much of the 20th century, research universities did not file patents in the biomedical arena, reflecting an ambivalence about limiting access to health research and discoveries.[7] This ambivalence faded during the 1970s, and the Bayh–Dole Act of 1980 both removed bureaucratic obstacles to patenting publicly funded research and gave congressional endorsement to the notion that academic patenting and licensing facilitated commercialization of university discoveries. The logic of the Bayh–Dole Act was that, without patents on academic discoveries—often "embryonic" in form and requiring additional development, including clinical trials—firms would lack incentives to develop them to the point where they were commercially useful. Under this theory, patents on academic research—which are then licensed to firms that develop and market the academic technologies—would promote "technology transfer."[8] In the decades following Bayh–Dole, academic patenting and licensing grew dramatically, with the bulk of this growth concentrated in the biomedical arena.[9] Academic institutions collect income on licensed patents, including sales-based royalties on products commercialized based on their patents. In the most recent year for which data are available, academic licensing income exceeded 1 billion US dollars.[10]

These activities have been surrounded by controversies, including debate about whether academic patents in fact are necessary for new product development; whether the presence of patent incentives distorts academic research agendas away from "basic" and toward "applied" research; whether they create conflict of interest in clinical research; and whether academic patents on "research tools" can hinder the progress of scientific research.[11,12]

The proposals just noted attempt to harness an *unintended* benefit from academic patenting of biomedical discoveries. By giving universities ownership rights over upstream discoveries, academic patents can give universities the power to compel licensees to not enforce these patents, or any follow-on patents, in developing countries, thus helping to promote access. This movement began in 2001, when, in response to demands from student and health activists, Yale University, the owner of the key patent on an important HIV treatment (stavudine), pressured Bristol-Myers Squibb, the licensee of this patent, to agree not to enforce the patent in South Africa.[13] This intervention reportedly led to a 30-fold reduction in the drug's price and a dramatic expansion of HIV treatment programs in South Africa.[14]

These developments were catalysts for the formation of Universities Allied for Essential Medicines, the campus chapters of which aim to persuade their parent universities to develop patent licensing policies that limit the ability of licensees to enforce academic patents (or related patents held by firms) in developing countries. These proposed licensing terms are generally modeled on the equitable access license developed by legal scholars.[15] The movement also led to the introduction of legislation in the US Senate: S. 4040, The Public Research in the Public Interest Act, sponsored by Senator Patrick Leahy (D, VT), which requires that, as a condition for receipt of federal funds, universities include in their licensing agreements clauses limiting the licensees' abilities to enforce academic patents—and the licensees' own patents on drugs with academic patents—against developing-country generic producers. Similar proposals have been endorsed by a range of international bodies, including the Association of American Medical Colleges, the World Health Organization, and the American Association of Arts and Sciences.[16]

Although this movement is intensifying, there is little empirical information on how large an impact such a strategy would have. Is the Yale case unique, or do academic institutions have ownership rights in a large number of drugs, making this strategy more generally feasible? In addition to citing specific cases in which universities owned key patents, the proposals discussed above are motivated by research showing that academic institutions play an important role in pharmaceutical innovation, drawing on bibliometric data,[17] case studies,[18,19] and survey evidence.[20] However, this previous research on the academic role in pharmaceutical innovation does not explicitly examine the extent to which academic institutions hold patents on the drugs, which is the relevant consideration for proposals to use university ownership of patents to attempt to affect prices and access. Academic research can affect industrial innovation through a range of channels: firms benefit from knowledge obtained through published academic articles and conference presentations, through collaborations with academic scientists, and through hiring trained graduate students. These channels of knowledge and technology transfer are generally not accompanied by patents held by universities. Accordingly, even if universities did significantly contribute to pharmaceutical innovation through these channels, because there are no patents, academic institutions can have little control over the pricing or dissemination of resulting drugs. That is, the broad research on the academic influence on drug development is not directly relevant for considerations of whether universities can help affect access; the salient consideration is whether universities hold patents on their contributions.

For proposals to use university ownership of drug patents to affect drug prices (and access) in developing countries to be feasible, two things would need to be true for such proposals to be reasonable. First, universities would have to own patents on a substantial number of drugs, and second, universities or firms licensing university technologies would have to currently be filing patents in developing countries. If the first statement were false, the proposed interventions would have little effect. If the second were false, the interventions would not be needed. I provide data on these issues.

METHODS

To examine these issues, I began by collecting information on

all drugs approved by the US Food and Drug Administration (FDA) between 1988 and 2005 from the FDA's online database,[21] which contains data on all FDA-approved drugs, including drug name and ingredient. I focused attention on the 1546 new drug applications approved between 1988 and 2005. "New" drug approvals include not just new molecular entities but also new derivatives of existing molecules, new formulations, new combinations of already approved compounds, and new indications, among other types of drugs. Unfortunately, by focusing on new drug applications, I did exclude numerous biotechnology drugs, which occasionally are filed as biological license agreements rather than new drug applications and thus are not subject to the requirements to list patents in the *Orange Book*.[22] Because the public sector role could be more pronounced for biotechnology drugs, this is a limitation of the current sample. I hope to explore this in future research with other sources of drug patent data.

To facilitate interpretation, I classified these new drug applications by approval year cohorts: 1988 to 1993, 1994 to 1999, and 2000 to 2005. To examine potential differential roles of public sector patents across different types of drugs, I analyzed new molecular entity and other new drug approvals separately. I also determined whether each of the drugs was given "priority review" by the FDA, which is granted when it is "A drug that appears to represent an advance over available therapy."[23] Some have argued that new molecular entities that receive priority review represent higher levels of innovativeness than do other drugs,[24] although this has been disputed by others.[25] Given the particular importance of HIV/AIDS drugs in the policy debates discussed above and the particular burden of this disease in developing countries,[26] I also specifically identified those new drug applications designated by the FDA as "drugs used in the treatment of HIV infections."[27]

Information on patents on FDA-approved drugs was collected from the February 2007 edition of the FDA's *Orange Book*.[22] Because the current *Orange Book* lists only unexpired patents, I supplemented this with legacy data obtained from older editions, dating back to 1988. I collected information on who owned each of these patents from the United States Patent and Trademark Office's Cassis database of bibliographic information from US patents,[28] and determined which of these owners were academic institutions, nonprofit research institutes, government laboratories, and hospitals using the Azoulay–Michigan–Sampat concordance.[29] I refer to these as "academic" patents in the analyses that follow.

I also examined which of the patents in the *Orange Book* were also filed in developing countries with data from the Derwent Innovation Index.[30] The Derwent database contains information on patent applications in 95 countries. Although the Derwent data may be somewhat noisy, especially for developing countries, it is generally considered the most comprehensive source of data on international patent protection. However, because this data set may miss potential filings, the statistics on international patent filings should be interpreted as lower bounds. I used World Bank classifications based on per capita gross domestic product levels[31] to classify 27 of these as low income or lower-middle income (India, Kenya, North Korea, Mongolia, Malawi, Nigeria, Vietnam, Zambia, Zimbabwe, Bulgaria, Brazil, China, Colombia, Cuba, Egypt, Indonesia, Iraq, Iran, Jordan, Sri Lanka, Morocco, Moldova, Peru, Philippines, Thailand, Tunisia, and Ukranian Republic).

RESULTS

Overall Trends

Figure 1 shows the number of new drug approvals over time, distinguishing between new molecular entities that received priority review, new molecular entities that did not receive priority review, and new drug applications that were not new molecular entities. Consistent with previous research,[32] the majority of new drug approvals were not new molecular entities. In addition, the share of approvals that were new molecular entitys that received priority review—arguably the most "innovative" drugs—has been decreasing over time, from 16.3% in the 1988 to 1993 cohort, to 14.2% in 1994 to 1999 and to 11.5% in 2000 in 2005.

Drugs With Academic Patents

Overall, 938 (60.7%) of the new drug applications had at least 1 patent. New molecular entities were significantly more likely to have patents than were other new drug applications (79.5% vs 52.3%; $P<.01$). A drug can be associated with multiple patents, and a patent can cover multiple drugs. In total, the new drug applications in the sample were associated with 1947 patents. Of these, 96 (4.9%) were academic patents.

At the new drug application level, 72 (7.7%) of drugs approved over this period had an academic patent. However, new molecular entities were significantly more likely to have an

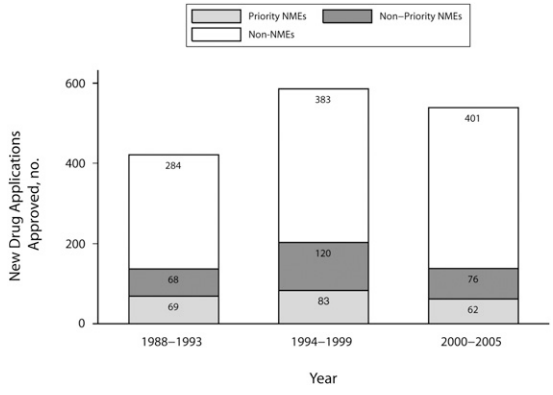
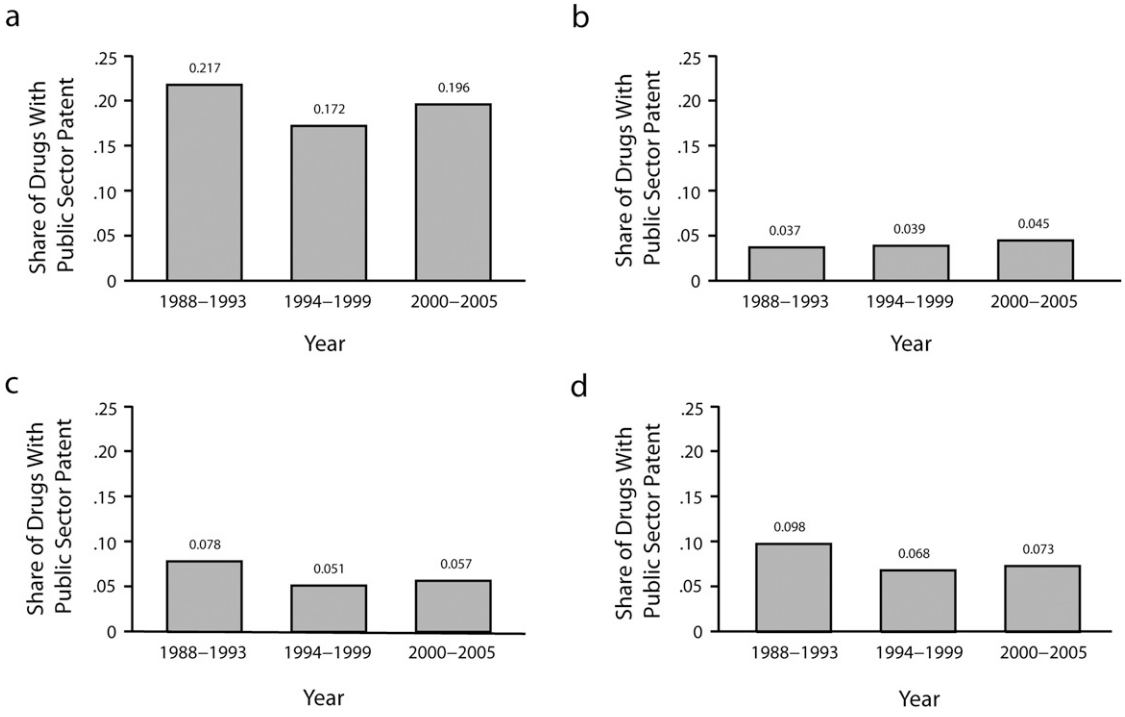


FIGURE 1—Approvals over time of priority new molecular entity (NME) drugs, nonpriority NME drugs, and non-NME drugs: 1988–2005.



Note. NME = new molecular entity.

FIGURE 2—Share of public sector patents, by year, going to (a) priority NME drugs, (b) nonpriority NME drugs, (c) non-NME drugs, and (d) all drugs: 1998–2005.

academic patent than were other new drug applications, with 10.3% having at least 1 academic patent compared with 5.9% for non–new molecular entities ($P<.001$). Additionally, 19.2% of priority new molecular entities had at least 1 academic patent compared with 4.02% of nonpriority new molecular entities ($P<.01$). Figure 2 shows trends over time and by chemical type. Although no sharp trends over time stand out, note that, consistently throughout this period, about 1 in 5 of the new molecular entities receiving priority approval had an academic patent.

Table 1 lists the 72 drugs with an academic patent, with the new drug application number, drug name, chemical type, approval year, and the academic institution or hospital owning patents on the drug. Several points stand out. First, whereas in most cases, academic institutions held patents bearing on 1 drug application associated with a molecule (typically the new molecular entity), in some cases, the academic patents also extend to follow-on drug applications (as previously discussed, because my unit of analysis was an new drug application, the same trade name or ingredient can appear with multiple new drug applications in this Table 1 [e.g., for different forms or dosages]). For example, for the HIV drug, stavudine, Yale's patent is listed in the *Orange Book* for the original new molecular entity application (approved in 1994) but also for the subsequent approvals for the oral solution formulation (approved in 1996) and the extended-release formulation (approved in 2002).

Second, 35 distinct institutions accounted for the "academic" patents on the 72 drugs, and the subset of 39 drugs with academic patents that were new molecular entities were associated with 26 patent holders. That is, ownership of the public sector patents is relatively diffuse.

A third interesting feature of Table 1 is the prominence of HIV/AIDS drugs. Twelve of the 72 drugs with academic patents were HIV/AIDS drugs (about 16.7%), whereas, overall, HIV/AIDS drugs accounted for 47 of the 938 new drug applications with patents approved over the period examined (5.01%). To consider this another way, whereas the share of non–HIV drugs with academic patents was 6.7%, the corresponding share for HIV drugs was 25.5%.

Patent Filings in Developing Countries

The first column of Table 2 shows that, of the 1947 unique patents listed in the *Orange Book*, 43% (830) were filed in developing countries. Firms were significantly more likely than were academic institutions to file patents in

TABLE 1—Drugs Approved by the US Food and Drug Administration With Academic Patents: 1988–2005

NDA No.	Tradename (Ingredient)	Approval Year	Public Sector Patent Holder
20 212	Zinecard (dexrazoxane hydrochloride)[a]	1995	New York University
20 412	Zerit (stavudine)[a]	1994	Yale University
20 413	Zerit (stavudine)	1996	Yale University
21 453	Zerit XR (stavudine)	2002	Yale University
20 819	Zemplar (paricalcitol)[b]	1998	University of Wisconsin
21 606	Zemplar (paricalcitol)	2005	University of Wisconsin
21 636	Zegerid (omeprazole; sodium bicarbonate)	2004	University of Missouri
21 706	Zegerid (omeprazole; sodium bicarbonate)	2004	University of Missouri
20 597	Xalatan (latanoprost)[a]	1996	Columbia University
20 961	Vitravene Preservative Free (fomivirsen sodium)[a]	1998	US Government, HHS
20 569	Vitrasert (ganciclovir)	1996	University of Kentucky
21 119	Visudyne (verteporfin)[a]	2000	Massachusetts General Hospital
20 154	Videx (didanosine)[a]	1991	US Government, HHS
20 155	Videx (didanosine)	1991	US Government, HHS
20 156	Videx (didanosine)	1991	US Government, HHS
21 183	Videx ec (didanosine)	2000	US Government, HHS
21 267	Vfend (voriconazole)	2002	University of Kansas
21 602	Velcade (bortezomib)[a]	2003	US Government, HHS
19 981	Ultratag (technetium TC-99M red blood cell kit)	1991	Associated Universities Inc.
21 752	Truvada (emtricitabine; tenofovir disoproxil fumarate)	2004	Emory University
20 408	Trusopt (dorzolamide hydrochloride)[a]	1994	University of Florida
21 248	Trisenox (arsenic trioxide)[a]	2000	Sloan-Kettering
20 505	Topamax (topiramate)[b]	1996	New England Medical Center
20 844	Topamax Sprinkle (topiramate)	1998	New England Medical Center
20 898	Thyrogen (thyrotropin alfa)[a]	1998	Sloan-Kettering
20 785	Thalomid (thalidomide)[a]	1998	Children's Hospital Boston
20 262	Taxol (paclitaxel)[a]	1992	US Government, HHS
21 055	Targretin (bexarotene)[a]	1999	SRI International
19 836	Supprelin (histrelin acetate)[a]	1991	Salk Institute
19 890	Stadol (butorphanol tartrate)	1991	University of Kentucky
20 657	Sporanox (itraconazole)	1997	US Government, HHS
21 106	Somavert (pegvisomant)[a]	2003	Ohio University
19 608	Sildaflo (silver sulfadiazine)	1989	Research Corporation
21 544	Seasonale (ethinyl estradiol; levonorgestrel)	2003	Medical College of Hampton Roads
21 320	Plenaxis (abarelix)[a]	2003	Indiana University
20 958	Pepcid Complete (calcium carbonate; famotidine; magnesium hydroxide)	2000	Brigham and Women's Hospital
19 880	Paraplatin (carboplatin)[a]	1989	Research Corporation (on behalf of Michigan State University)
20 886	Panretin (alitretinoin)[a]	1999	Salk Institute
19 927	Nizoral (ketoconazole)	1990	University of Tennessee
20 310	Nizoral A-D (ketoconazole)	1997	University of Tennessee
20 326	Neutrexin (trimetrexate glucuronate)[a]	1993	US Government, HHS
21 487	Namenda (memantine hydrochloride)[b]	2003	Children's Hospital Boston

Continued

TABLE 1—*Continued*

20 586	Meretek UBT kit (with pranactin) (urea, C-13)[b]	1996	Baylor College of Medicine
21 674	Menostar (estradiol)	2004	University of California
21 446	Lyrica (pregabalin)[a]	2004	Northwestern University
20 845	Inomax (nitric oxide)[a]	1999	Massachusetts General Hospital
20 199	Hivid (zalcitabine)[a]	1992	US Government, HHS
20 076	Habitrol (nicotine)	1991	University of California
20 637	Gliadel (carmustine)	1996	Massachusetts Institute of Technology
19 863	Geref (sermorelin acetate)[b]	1990	Salk Institute
20 443	Geref (sermorelin acetate)	1997	Salk Institute
21 481	Fuzeon (enfuvirtide)[a]	2003	Duke University
20 038	Fludara (fludarabine phosphate)[a]	1991	US Government, HHS
20 195	Fentanyl (fentanyl citrate)	1993	University of Utah
20 044	Exosurf neonatal (cetyl alcohol; colfosceril palmitate; tyloxapol)[a]	1990	University of California
19 677	Enlon-plus (atropine sulfate; edrophonium chloride)	1991	University of California
21 500	Emtriva (emtricitabine)[b]	2003	Emory University
21 896	Emtriva (emtricitabine)	2005	Emory University
20 193	Elmiron (pentosan polysulfate sodium)[b]	1996	University of California
21 283	Diovan (valsartan)	2001	Brigham and Women's Hospital
20 869	Cosopt (dorzolamide hydrochloride; timolol maleate)	1998	University of Florida
21 673	Clolar (clofarabine)[a]	2004	Southern Research Institute
21 197	Cetrotide (cetrorelix)[b]	2000	Tulane University
19 829	Ceretec (technetium TC-99M exametazime kit)[a]	1988	University of Missouri
19 785	Cardiolite (technetium TC-99M sestamibi kit)[b]	1990	Harvard College
20 954	Busulfex (busulfan)	1999	University of Texas
20 404	Avita (tretinoin)	1997	University of California
21 316	Altoprev (lovastatin)	2002	Children's Hospital Boston
21 462	Alimta (pemetrexed disodium)[a]	2004	Princeton University
19 937	Adenocard (adenosine)[a]	1989	University of Virginia
20 747	Actiq (fentanyl citrate)	1998	University of Utah
20 162	Acthrel (corticorelin ovine triflutate)[a]	1996	Salk Institute

Note. HHS = US Department of Health and Human Services; NDA = new drug application.
[a]New molecular entity that received priority approval.
[b]New molecular entities that did not receive priority approval.

developing countries: 43.9% of nonacademic patents were filed in developing countries, compared with 18.75% of academic patents ($P<.01$).

The equitable access license and other policy initiatives discussed previously have a "viral" component, aimed at limiting not only enforcement of academic patents in developing countries, but also the ability of firms to enforce any of their own patents on the same drugs in developing countries. Accordingly, it is also interesting to examine firms' international filing strategies for their own patents on drugs that also have at least 1 academic patent.

Overall, 81 of the firms' 1851 patents were on drugs that also had academic patents. The next 2 rows of Table 2 show the share of firms' patents filed in developing countries in cases in which there was an academic patent on the same drug (row 4), and in cases in which there were not (row 5). Although firms were more likely to file patents in developing countries in cases in which academic institutions did not have patents on the same drugs, the difference was qualitatively small and statistically insignificant (39.5% vs 44.1%; $P=.42$).

Before the signing of the TRIPs agreement in 1995, product patents on drugs were not allowed in many developing countries. In addition, patent data in developing countries may be more complete in recent years than was previously the case. Accordingly, I also

TABLE 2—Share of Drugs Approved by the US Food and Drug Administration Between 1988 and 2005 With Patent Applications in Developing Countries

	Overall		Filed Pre-1996		Filed 1996 or Later	
	Mean (SE)	No.	Mean (SE)	No.	Mean (SE)	No.
All patents	0.43 (0.01)	1947	0.35 (0.01)	1414	0.64 (0.02)	533
Academic patents	0.19 (0.04)	96	0.14 (0.04)	80	0.43 (0.13)	16
Nonacademic patents	0.44 (0.01)	1851	0.40 (0.01)	1334	0.64 (0.02)	517
Nonacademic patents with academic patents on same drug	0.40 (0.05)	81	0.29 (0.06)	55	0.62 (0.09)	26
Nonacademic patents without academic patents on same drug	0.44 (0.01)	1770	0.36 (0.01)	1279	0.65 (0.02)	491

Note. Mean values are percentage of drugs filed in developing countries.

examined pre- and post-1995 filed patents separately in the second and thirds columns of Table 2. For each of the groups, there was a qualitatively and statistically significant ($P<.05$ for all rows) increase over time in the propensity to file in developing countries. Overall, in the post-1995 cohort of patents, the share of academic drug patents filed in developing countries was 43.8%, compared with 64.4% of nonacademic drug patents. Although the difference was not statistically significant at conventional levels ($P=.09$), this could reflect the relatively small number of post-1995 academic patents in the sample. Also, as with the overall sample, there was no statistically significant difference between the nonacademic patents on drugs that also had academic patents and other, nonacademic patents (61.5% vs 64.6%; $P=.75$).

DISCUSSION

The data show that the stavudine case discussed previously is not unique. The overall share of drugs approved between 1988 and 2005 on which universities own patents was relatively low—7.7%—and the share for new molecules was only slightly higher—10.3%. However, universities own patents on nearly 1 in 5 (19.2%) of the drugs that are arguably the most innovative—new molecular entities that received "priority" approval by the FDA; this share has been basically stable since the late 1980s. In addition, universities own key patents on over one quarter of the HIV/AIDS drugs approved since 1988, which is particularly important given the potentially catastrophic impact of this disease in the developing world. The data do not support the arguments of some critics of drug companies[33] that the bulk of important pharmaceutical innovation is done by the public sector. However, they do suggest that a nontrivial fraction of marketed drugs, particularly those that may be considered the most novel and clinically useful, emanate from and are patented by universities and hospitals.

The results also suggest that universities, and the firms that commercialize and market drugs with academic patents, currently apply for patents in developing countries. For patents filed after 1995, at least 44% of academic patents, and 62% of firms' patents on drugs with academic patents, were filed in developing countries.

Taken together, these findings suggest that changes to university policies could have important effects and provide evidence of the feasibility of using academic control of key drug patents to promote access in developing countries.

What about the desirability of exercising this control? What are the costs, what are the risks? I believe that the main potential downside risk of exercising this control is that potential licensee firms would balk at these provisions, choosing not to license and develop drugs that they would have done in the absence of restrictions on enforcing patents in developing countries. As discussed previously here, the logic underlying academic patenting and licensing, expressed in the Bayh–Dole Act, is that firms need the promise of monopoly power to have incentives to develop, test, and commercialize university-developed inventions.

By limiting profits from developing countries, would the proposals discussed here hinder incentives to bring academic inventions to market? This seems unlikely, since developing countries represent a trivial proportion of consumption of most pharmaceuticals.[34] For drugs against "global" diseases, like cancer, diabetes, cardiovascular disease, and HIV/AIDS, firms rely on markets in developed countries for the bulk of their profits.[35] Accordingly, contractual limits on firms' abilities to enforce patents in developing countries would not strongly affect their incentives to commercialize most academic inventions. Paradoxically, the cases in which such limits would be most likely to deter commercialization would be those in which markets in developing countries represent the bulk of potential consumption (i.e., drugs targeted specifically at "neglected" diseases—those without large markets in developed countries). However, very few drugs for neglected diseases are developed and marketed by pharmaceutical companies in the current environment,[36,37] and there is relatively little public

funding in developed countries for neglected-disease research.[38] Neglected diseases are an important, but separate, policy problem.

Even though firms would not rationally walk away from licensing drugs on global diseases if subjected to limits on enforcing patents in developing countries, they may threaten to do so in bargaining over licensing terms. In addition, firms, not universities, likely have stronger bargaining power in licensing negotiations: for most academic inventions, the modal number of licensees expressing interest is zero.[38] Given the small number of suitors for most academic patents, individual academic institutions may be unwilling or unable to commit to imposing demands on potential licensees. In this context, top-down requirements from the funders of this research (e.g., those in the Leahy bill) may be necessary to change licensing policies and practices. More generally, the data in the previous sections show that academic ownership of patents on FDA-approved drugs is dispersed across a large number of institutions. It may be difficult, even with strong campus-level activism, to bring about any change at all in the licensing policies of these institutions, or that of other academic institutions that may generate new pharmaceuticals in the future. This too suggests that top-down legislative approaches may be more fruitful in changing academic licensing practices.

Although the results reported in this paper suggest that universities could play a role in enhancing access to drugs, the magnitude of their potential impact remains unclear. Difficulties in obtaining drug consumption data from developing countries make it hard to know the extent to which the university-developed drugs identified here are important for public health in the developing world. Nor is it possible to know the extent to which patents, vis-à-vis other factors, currently inhibit access to these drugs, and thus, the magnitude of the global health impacts that changes in academic licensing policies would have. In-depth (qualitative and quantitative) case study research exploring these issues—oriented around the drugs listed in Table 1—is an important task for future research. ■

About the Author

Bhaven N. Sampat is with the Department of Health Policy and Management, the International Center for Health Outcomes and Innovation Research, and the School of International and Public Affairs, Columbia University, New York, NY.

Requests for reprints should be sent to Bhaven N. Sampat, PhD, Columbia University, 600 West 168th St, 7th Floor, New York, NY 10032 (e-mail: bns3@columbia.edu).

This essay was accepted April 2, 2008.

Acknowledgments

This work was funded in part by grants from the Ford Foundation and the Robert Wood Johnson Foundation.

The author thanks Orin Herskowitz, Amy Kapczynski, Arti Rai, Michael Steffen, and Robynn Sturm for thoughtful comments on this research.

End Notes

1. HIV-AIDS, Malaria, TB, and Access to Essential Medicines Working Group. "Prescription for Healthy Development: Increasing Access to Medicines." London: Earthscan, 2005.

2. Pierre Chirac and Els Torreele, "Global framework on essential health R&D." *Lancet* 367, no. 9522 (May 13, 2006): 1560–1561.

3. Amir Attaran and Lee Gillespie-White. "Do Patents for Antiretroviral Drugs Constrain Access to AIDS Treatment in Africa?" *Journal of the American Medical Association* 286, no. 15 (October 17, 2001): 1886–1892.

4. Universities Allied for Essential Medicines Web site, http://www.essentialmedicine.org (accessed March 1, 2008).

5. S. Chaudhuri, *The WTO and India's Pharmaceuticals Industry: Patent Protection, TRIPS, and Developing Countries* (New York, NY: Oxford University Press, 2005).

6. Ibid.

7. David C. Mowery and Bhaven N. Sampat, "University Patents and Patent Policy Debates in the USA, 1925–1980," *Industrial and Corporate Change* 10, no. 3 (2001): 781–814.

8. David Mowery, Richard Nelson, Bhaven Sampat, Arvids Ziedonis, *Ivory Tower and Industrial Innovation: University-Industry Technology Transfer Before and After the Bayh-Dole Act* (Stanford, CA: Stanford Business Books, 2004).

9. Pierre Azoulay, Ryan Michigan, Bhaven N. Sampat, "The anatomy of medical school patenting," *New England Journal of Medicine* 357, no. 20 (November 15, 2007): 2049–2056.

10. *AUTM Licensing Survey 2006* (Norwalk, CT: Association of Technology Licensing Managers, 2006).

11. Mowery, Nelson, Sampat, and Ziedonis, *Ivory Tower and Industrial Innovation.*

12. Azoulay, Michigan, and Sampat, "The anatomy of medical school patenting," 2049–2056.

13. D. Lindsey, "Amy and Goliath," *Salon* (2001) http://archive.salon.com/news/feature/2001/05/01/aids (accessed March 1, 2008).

14. Dave A. Chokshi, "Improving access to medicines in poor countries: the role of universities," *PLoS Medicine* 3, no. 6 (June 1, 2006): e136.

15. Amy Kapczynski, Samantha Chaifetz, Zachary Katz, Yochai Benkler, "Addressing global health inequities: an open licensing approach for university innovations," *Berkeley Technology Law Journal* 20, no. 2 (2005): 1031–1114.

16. Dave A. Chokshi and Rahul Rajkumar, "Leveraging university research to advance global health," *Journal of the American Medical Association* 298, no. 16 (October 24, 2007): 1934–1936.

17. Steven G. McMillan, Francis Narin, and David L. Deeds, "An analysis of the critical role of public science in innovation: the case of biotechnology," *Research Policy* 29, no. 1 (2000): 1–8.

18. Iain Cockburn, Rebecca Henderson, "Public–private interaction in pharmaceutical research," *Proceedings of the National Academy of Sciences of the U S A* 93, no. 23 (November 12, 1996): 12725–12730.

19. *The Benefits of Medical Research and the Role of the NIH* (Washington, DC: US Congressional Joint Economic Committee, 2000).

20. Wesley M. Cohen, Richard R. Nelson, John P. Walsh. "Links and impacts: the influence of public research on industrial R&D" *Management Science* 48, no. 1 (2002): 1–23.

21. US Food and Drug Administration, Drugs@FDA Web site, http://www.accessdata.fda.gov/Scripts/cder/DrugsatFDA (accessed August 7, 2008).

22. *Approved Drug Products with Therapeutic Equivalence Evaluations*, 22nd ed (Washington, DC: US Department of Health and Human Services, 2007) http://www.fda.gov/cder/ob (accessed August 7, 2008).

23. US Food and Drug Administration, Drugs@FDA Web site, question 12, http://www.fda.gov/cder/drugsatfda/faq.htm#chemtype_reviewclass (accessed August 7, 2008).

24. National Institute for Health Care Management, *Changing Patterns of Pharmaceutical Innovation* (Washington, DC: National Institute for Health Care Management, 2002).

25. PhRMA. "NIHCM's Report on Pharmaceutical Innovation: Fact vs. Fiction," http://mednet3.who.int/prioritymeds/report/append/8342.pdf (accessed February 20, 2008).

26. TC Quinn, "Global burden of the HIV pandemic," *Lancet* 348, no. 9020 (1996): 99–106.

27. Food and Drug Administration, "Drugs used in the treatment of HIV infection," http://www.fda.gov/oashi/aids/virals.html (accessed February 20, 2008).

28. United States Patent and Trademark Office's Cassis database of bibliographic information from US patents, http://www.uspto.gov/web/offices/ac/ido/

oeip/catalog/products/cassis.htm (accessed September 4, 2008).

29. Azoulay, Michigan, and Sampat, "Anatomy of Medical School Patenting," 2049–2056.

30. Devwent Innovation Index, http://scientificthomsonreuters.com/products/dii (accessed September 1, 2008).

31. The World Bank, "A short history," http://go.worldbank.org/U9BK7IA1J0 (accessed February 20, 2008).

32. See note 15 above.

33. Marcia Angell, *The Truth About Drug Companies: How They Deceive Us and What to Do About It* (New York, NY: Random House, 2004).

34. Kapczynsi, Chaifetz, Katz, and Benkler, "Addressing global health inequities," 1031–1114.

35. J. Lanjouw, "A patent policy for global diseases," *Innovations* 1, no. 1 (2006): 108–114.

36. See note 2 above.

37. Michael Kremer and Rachel Glennerester, *Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases* (Princeton, NJ: Princeton University Press, 2004).

38. J. Lanjouw and M. McLeod, "Pharmaceutical R&D for low-income countries: global trends and participation by Indian firms," *Economic and Political Weekly* 40, no. 39 (September 24, 2005): 4232–4242.

39. Jensen, Thursby, and Thursby, "Disclosure and licensing of university inventions: the best we can do with the sh*t we get to work with," *International Journal of Industrial Organization* 21, no. 9 (2003): 1271–1300.

The Scientific Basis for Law as a Public Health Tool

Anthony D. Moulton, PhD, Shawna L. Mercer, PhD, Tanja Popovic, MD, PhD, F(AAM), AM(AAFS), Peter A. Briss, MD, MPH, Richard A. Goodman, MD, JD, MPH, Melisa L. Thombley, JD, MPH, Robert A. Hahn, PhD, MPH, and Daniel M. Fox, PhD

Systematic reviews are generating valuable scientific knowledge about the impact of public health laws, but this knowledge is not readily accessible to policy makers. We identified 65 systematic reviews of studies on the effectiveness of 52 public health laws: 27 of those laws were found effective, 23 had insufficient evidence to judge effectiveness, 1 was harmful, and 1 was found to be ineffective. This is a valuable, scientific foundation—that uses the highest relevant standard of evidence—for the role of law as a public health tool.

Additional primary studies and systematic reviews are needed to address significant gaps in knowledge about the laws' public health impact, as are energetic, sustained initiatives to make the findings available to public policy makers. (*Am J Public Health.* 2009;99:17–24. doi:10.2105/AJPH.2007.130278)

LAW IS A TRADITIONAL PUBLIC health tool that has made vital contributions to the major public health achievements of the 20th century. Examples include school immunization laws that helped reduce the rates of infectious disease and tobacco control laws that helped reduce the rates of chronic disease.[1] Indeed, many, if not all, government public health endeavors rely on laws crafted to address specific health conditions or risk factors ("interventional" public health laws), laws that create and empower public health agencies and jurisdictions ("infrastructural" public health laws), or the general police powers of state governments. In addition, many laws not designed principally for public health objectives nonetheless have public health consequences (e.g., taxation and education laws). While potentially powerful legal tools for public health, these latter laws are not considered here.

Policy makers weigh many factors as they consider adopting and promoting public health laws. A central question—especially in this time of emphasis on evidence-based practice and policy—is whether there is sound scientific evidence that a given public health law is effective. The number of peer-reviewed publications reporting on the impact of interventional public health laws is growing, as is the number of systematic reviews and meta-analyses of such primary studies.[2] However, this body of scientific knowledge, although potentially of great value, to date has not been summarized and made readily accessible to policy makers. We begin to address this gap.

Systematic reviews and meta-analyses apply the most sophisticated methodologies currently available to assess the findings of multiple primary studies focused on a given intervention.[3] Systematic reviews have been defined as

> review[s] of a clearly formulated question that use[s] systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyze data from the studies that are included in the review.[4]

Often considered a subset of systematic reviews, meta-analyses are

> quantitative statistical analyses . . . applied to separate but similar experiments of different and usually independent researchers and that involve[s] pooling the data and using the pooled data to test the effectiveness of the results.[5]

For the sake of simplicity, we use the term "systematic review" for both.

We report on a survey of systematic reviews of peer-reviewed primary studies of individual interventional public health laws. It is thus a report on the highest-quality scientific evidence currently available on the effectiveness of such laws. In addition, we identified recommendations contained in those reviews for future research on interventional public health laws.

METHODS

We defined interventional public health laws as constitutional or statutory measures, regulations,