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Priority Review Vouchers – A Piece of the Incentive Puzzle

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ABSTRACT

On September 27, 2007, a program designed to encourage innovation for the development of drug treatments for tropical diseases, traditionally neglected by researchers and developers, was signed into law. Novel treatments that meet FDA approval are awarded a second, transferable priority review voucher that could shave several months off the FDA review process for a non-priority drug therapy. The recipient may use the voucher or transfer it to a third party seeking priority review for a non-qualifying drug entity. This paper reviews the priority review voucher incentive against a backdrop of other patent and non-patent incentive mechanisms already in existence, including stronger patent enforcement and patent buyouts or prizes. The first section briefly describes the market incentive of the United States' patent system and gaps in innovation that occur absent the market incentive. The next section examines the limited market incentives and substantial investment costs that discourage research for neglected diseases in the pharmaceutical industry. The last sections of the paper describe and review various proposals to increase incentive and to drive innovation where none currently exists, with the final section describing and defending the priority review voucher mechanism. The paper concludes that no single proposal goes far enough to bridge gaps left by the patent system, but that each mechanism should be used concurrently to push and pull innovation along.

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PRIORITY REVIEW VOUCHERS AND THE CASE OF NOVARTIS' COARTEM

In the short span of eighteen months, a policy paper written by three academic economists from Duke University made the rounds in Washington D.C. and became law in late September 2007. The law aimed to incentivize the development of drug treatments for neglected tropical diseases by providing vouchers redeemable for priority review from the Food and Drug Administration (hereinafter "FDA"). The voucher would be transferable, allowing the bearer an expedited review of a prospective, non-qualified drug and reducing the time to take the drug to market. Conceptually, diseases untouched by the medical miracles of the last fifty years would receive renewed attention from research bankrolled by the U.S. government and profit-seeking pharmaceutical companies.

Exactly who develops the innovation is immaterial as long as a new drug therapy is invented. Issues of distribution and low-cost access are beyond the scope of the primary legislative purpose to fill the innovation gap left in spite of the patent system. In April 2009, the Swiss pharmaceutical group Novartis acquired the first priority review voucher issued under the FDA program. It was issued for the combination drug Coartem (artemether and lumefantrine) which is used in the treatment of malaria.[1] At first glance, this is precisely the innovation lawmakers had in mind: Coartem is a highly effective treatment that discourages drug resistance through the use of two antimalarial agents.[2] How effective? Since its first use in 2001, over 200 million doses of Coartem have been administered in the developing world.[3] Herein lies the problem: there is no need to

[1] *News in Brief (First FDA Priority Review Voucher Awarded)*, 8 NATURE REVIEWS DRUG DISCOVERY 346, 347 (2009), *available at* http://www.nature.com/nrd/journal/v8/n5/pdf/nrd2895.pdf.

[2] Press Release, Novartis, Novartis Receives FDA Priority Review for Coartem (Sept. 15, 2008), http://www.novartis.com/newsroom/media-releases/en/2008/1251164.shtml.

[3] Andrew Jack, *Novartis Hopes Success with Malaria Will Aid Second Drug*, FIN. TIMES (Eur. Ed. 1), Dec. 5, 2008, Companies—International, at 23.

encourage an innovation already in wide use throughout the developing world.

Is Novartis' request for a priority review voucher for Coartem a proper use or a glaring abuse of the incentive system? One critic has called Novartis' action an abuse that will depreciate the future value of a voucher earned by another novel innovation.[4] Another critic called for Novartis to dedicate their windfall towards new neglected diseases research.[5] Novartis merely seeks the voucher "to accelerate review of another drug currently under development."[6]

Coartem was not developed with the priority review voucher in mind. One of the original authors of the policy paper, Jeffrey Moe, acknowledges that the first applicants for a qualifying voucher "will get them essentially by serendipity" because the program did not exist when the drugs being considered were in the product pipeline.[7] The voucher program already faces a wave of criticism: pharmaceutical companies question the ability of the FDA to meet the priority review requirements; policy planners question whether resources are properly allocated; and non-profit organizations question the accessibility and affordability of the encouraged innovation.

I. INTRODUCTION

A primary tension in international patent law is the balance between enforceable intellectual property protections and effective access to technologies in developing nations. This paper describes and evaluates methods currently used to facilitate the distribution of technologies, but will pay particular attention to efforts that preserve the innovative incentive that patent holders enjoy. Inseparable from a presentation of effective methods is an analysis of the consequences–both positive and negative–for existing and potential patent holders.

This paper will use examples from the pharmaceutical industry and will focus on three methods–stronger patent enforcement, patent buyouts/prizes, and a priority review voucher–that aim to encourage the development or distribution of pharmaceuticals while preserving the rights and economic incentives necessary to entice innovators.

The first section will briefly touch on the patent system within the United States and emphasize the historical precedent that formed the current landscape of intellectual property rights and obligations. The current patent system assumes that it can efficiently meet public demand by providing strong intellectual property protections and reserving

[4] Knowledge Ecology International, *KEI Comments to the Priority Review Voucher Mechanism* (Dec. 19, 2008), http://www.keionline.org (search "Priority Review Voucher"); *see* Tatum Anderson *Novartis Under Fire for Accepting New Reward for Old Drug*, 373 THE LANCET 1414 (2009).

[5] Rohit Malpani, *Robbing the Poor to Pay the Rich – Novartis' Christmas Gift to Itself!*, OXFAM INT'L BLOGS, Dec. 16, 2008, http://blogs.oxfam.org/en/blog/08-12-16-robbing-poor-pay-rich-novartis-christmas-gift-itself.

[6] Jack, *supra* note 3. Novartis did not need to seek FDA approval for coartem, but doing so may facilitate USAID's acquisition and distribution of the drug. USAID, *ADS Chapter 312—Eligibility of Commodities*—312.5.3c Pharmaceuticals, *available at* http://www.usaid.gov/policy/ads/300/312.pdf.

[7] Michael McCaughan, *Treat and Trade: The New Priority Review Voucher Market*, THE REG. POL'Y MARKET ACCESS REP., July-Aug. 2008, at 1, 9.

the economic right of market exclusivity to the patent holder. Because the patent system efficiency depends on a market incentive, however, there are innovation gaps where no market pull exists.

The second section will look at the gaps in innovation existing in the pharmaceutical industry. While it is difficult to justify the lack of investment in neglected disease research, the limited financial reward in those markets combined with a shift in the pharmaceutical industry to ever-increasing expense and reward cycles underscore an economic reality that has allowed for gaps in innovation.

The third section reviews different proposals to resolve the problem of insufficient pharmaceutical distribution and innovation. One such solution is the stronger enforcement of existing intellectual property rights to encourage knowledge transfer. Furthermore, more reliable enforcement will help develop a domestic knowledge industry more able to address local needs. Another potential solution is the use of a patent buyout system to create a market incentive where none currently exists or to encourage knowledge transfer. Similar to a patent buyout is a prize which shifts the value of innovation to the distribution, not restriction, of knowledge. All of these proposals are taken together as complementary to the overall goal of increased innovation and distribution.

The final substantive section will discuss a transferrable priority review voucher approved as part of the Food and Drug Administration Amendments Act of 2007. Applicants who develop new drug therapies to treat specified tropical diseases may acquire a secondary voucher for expedited FDA review that can be either used or sold. This scheme assumes that pharmaceutical firms will be eager to purchase such vouchers to save time in the regulation process. This section will look at some of the costs and benefits that may influence the success of the voucher program.

Optimal social utility–the best use of resources–requires a piecemeal approach. If a patent holder agrees to a patent buyout to license a drug treatment for a limited geographic area, the presence of parallel importation of generics in that area will undermine the patent holder's desire to repeat. Reliable enforcement of intellectual property rights is necessary. If no incentive exists to develop drug therapies to treat tropical diseases, a patent buyout will serve no purpose. Incentives are necessary to shift innovative capabilities to research on treatments for neglected diseases. If an innovator has successfully navigated a patent thicket and developed such a treatment, there is no social utility gained until the treatment reaches a population at risk of disease.

II. PROMOTING THE PUBLIC GOOD THROUGH A PRIVATE RIGHT

From its inception Congress has been entrusted to nurture innovation through grants of exclusive market power to patent recipients. The U.S. Constitution allows Congress "[t]o Promote the Progress of Science and useful Arts, by securing for limited Times to authors and Inventors the exclusive Right to their respective Writings and

Discoveries."[8] Like the Constitution, terms within the clause–such as "progress," "limited times," "discoveries"–are so general as to frustrate efforts to reach an unequivocal interpretation of Congressional scope or powers.[9] Nonetheless, Congress presumably had some authority to convey a monopoly right to an inventor. Even Thomas Jefferson, who was adamant "[t]hat ideas should freely spread from one to another over the globe, for the moral and mutual instruction of man, and improvement of his condition," allowed that "[s]ociety may give an exclusive right to the profits arising from them, as an encouragement to men to pursue ideas which may produce utility."[10] As noted above, the Founders recognized that invention led to utility and authorized Congress to confer an exclusive market right to encourage such invention.

A patent holder enjoys market-based exclusivity, but it is worth reviewing why and for what benefit this right is conferred. Thomas Jefferson–a member of the nascent patent board–argued that the privilege be limited only to those inventions "which are worth to the public the embarrassment of an exclusive patent."[11] The Supreme Court likewise recognized public policy as the reason for market exclusivity in *Martin Salt Co. v. G. S. Suppiger Co.* and reasoned that beyond the policy justification "the granted monopoly excludes from it all that is not embraced in the invention."[12] In *Graham v. John Deere Co.*, a decision rendered after the Patent Act of 1952, the Supreme Court reasoned that the patent power was restrained by the Constitution and that Congress may not "enlarge the patent monopoly without regard to the innovation, advancement or social benefit gained thereby."[13] Concerning the public policy benefit, similar arguments have been made in support of copyright–akin to patents because they share the same Constitutional clause. Most recently, the Supreme Court stated that copyright statutes, and by parallel reasoning, patent statutes, must: serve public, not private, interest; advance knowledge and learning; and may do so by providing incentives and removing limits on sharing upon the completion of a protected time period.[14] These precedents indicate that a patent's purpose always has been and continues to be to advance a public good through the conferral of a limited private economic privilege.

A patent's primary value is the market exclusivity of the named invention. The

[8] U.S. CONST. art. I, § 8, cl. 8.

[9] *See* Thomas B. Nachbar, *Intellectual Property and Constitutional Norms*, 104 COLUM. L. REV. 272 (2004) (questioning the conventional interpretation of scope and authority authorized in the intellectual property clause of the U.S. Constitution).

[10] Letter from Thomas Jefferson to Isaac McPherson (Aug. 13, 1813), *in* 13 THE WRITINGS OF THOMAS JEFFERSON, at 334 (Andrew A. Lipscomb & Albert E. Branch, eds., Library ed. 1904).

[11] *Id.* at 335.

[12] Morton Salt Co. v. G. S. Suppiger Co., 314 U.S. 488, 492 (1942); *see also* Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225 (1964) (arguing the patent privilege should be limited to guard the rights and welfare of community); Mercoid Corp. v. Mid-Continent Inv. Co., 320 U.S. 661 (1944) (finding the patent privilege is conditioned on public purpose); Roberts v. Sears, Roebuck & Co., 697 F.2d 796 (7th Cir. 1983) (disfavoring a patent for an invention that "would confer no benefits that might offset the cost of monopoly").

[13] Graham v. John Deere Co. of Kan. City, 383 U.S. 1, 6 (1966). *But see* Nachbar, *supra* note 9, at 328 (arguing that the Framers did not adopt Jefferson's "general abhorrence of monopolies").

[14] Eldred v. Ashcroft, 537 U.S. 186, 247-248 (2003).

value of such a right was recognized early by the Supreme Court,[15] which later compared the cost of granting such a patent privilege to a toll exacted from the public.[16] The treatment of the patent right as personal property also creates value as the patent holder is at liberty to exclude others from its use or to exchange the privilege for some valuable good. While public policy may justify the issue of a patent, U.S. patent law does not require the patent holder to make, use, or vend the invention;[17] force a compulsory license of the patent;[18] or impinge on the validity of a patent due to disuse.[19] These are some of the basic assumptions of United States patent law—essentially a market-based tool—that will be used later for comparison with non-patent market-based alternatives.

Though simplistic, the above review of patent purposes outlines the foundation of a system of incentive and protection that has ably encouraged significant innovation in a diverse range of productive ventures. In the United States, the patent model has been very successful in adding value to innovation.[20] Intellectual property protection remains immensely important to the U.S. economy, with intellectual property comprising an estimated 45% of national GDP.[21] Intellectual property protection was not, however, always valued. The next section focuses on the historical shift in the U.S. to an ever-increasing patent protection regime within the context of the pharmaceutical industry.

III. VALUE IN KNOWLEDGE BUT NO VALUE WITHOUT A MARKET

Without the market exclusivity and protections of patented property, researchers would not likely invest significant time and resources to develop modern drug therapies.[22] While there is some debate as to the cost of developing a single successful drug,[23] the United States' consistent enforcement of intellectual property rights makes

[15] *Ex parte* Wood & Brundage, 22 U.S. 603, 608 (1824) ("The inventor has, during this period, a property in his inventions; a property which is often of very great value, and of which the law intended to give him the absolute enjoyment and possession.").

[16] Great Atl. & Pac. Tea Co. v. Supermkt. Equip. Corp., 340 U.S. 147, 154 (1950).

[17] Woodbridge v. United States, 263 U.S. 50, 55 (1923).

[18] Hartford-Empire Co. v. United States, 323 U.S. 386 (1945). *But see* eBay v. MercExchange, L.L.C., 547 U.S. 388 (2006) (finding an injunction shall not issue solely on validity of the patent and evidence of infringement).

[19] Special Equip. Co. v. Coe, 324 U.S. 370 (1945).

[20] European Patent Office, SCENARIOS FOR THE FUTURE 15 (European Patent Organisation 2007).

[21] *Id*. at 53.

[22] Richard E. Levin et al., *Appropriating the Returns from Industrial Research & Development*, 3 BROOKINGS PAPERS ON ECON. ACTIVITY 783 (1987).

[23] Joseph DiMasi & Henry Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 MANAGERIAL & DECISION ECON. 469, 470 (2007) ("estimated to average in excess of $800 million"); Kevin Outterson, *Patent Buy-Outs for Global Disease Innovations for Low- and Middle-Income Countries*, 32 AM. J. L. AND MED. 159, 159-160 (2006) ("Patented pharmaceuticals may be priced at more than 30 times the marginal cost of production."); Public Citizen, *Critique of the DiMasi/Tufts Methodology and Other Key Prescription Drug R&D Issues*, http://www.citizen.org/congress/reform/drug_industry/articles.cfm?ID=6532 (last visited June. 11, 2009) ("[T]he average after-tax cash outlay for a self-originated NCE is approximately $240 million.").

any investment made there by innovators less risky.[24]

The commitment to protecting intellectual property rights in the United States has not always been as strong as it is today. During the early twentieth century, the American Pharmaceutical Association—truly, an association of pharmacists—protested "unfair competition from abroad" because German firms held many American chemical patents.[25] Congress did not loosen patent laws, however, and efforts at reform seemed to dissipate after America joined World War I and 4,500 German-owned chemical patents were expropriated and sold at a substantial discount to domestic firms.[26] Efforts to broaden the scope of patentable innovation increased as scientific knowledge grew. Most notably, a patent was awarded for the antibiotic streptomycin and for a process for producing it with bacteria, though the bacteria itself "was a natural product that could hardly have been invented by the Merck scientist named in the patent."[27]

As innovation yields products and innovators seek to protect investments and extract value from them, strong intellectual property rights and the enforcement of those rights becomes a priority. Curiously, a developing country may perceive a benefit from maintaining weak intellectual property rights. For example, a country may appropriate protected intellectual property, thereby creating a domestic industry, and would be "doing nothing more than following historically proven methods for advancing development."[28] Rather than condoning the appropriation of intellectual property, however, this discourse shows the difficulty of demanding strong intellectual property rights absent any incentive to protect such rights.[29] Simply put, the need for strong intellectual property rights must outweigh the need for weak intellectual property rights before progress is made.

Within the United States, efforts have been made to expand access to pharmaceutical products while preserving the economic incentive for innovation. In 1984, Congress passed the Drug Price Competition and Patent Term Restoration Act (also known as the Hatch-Waxman Act) for the purpose of lowering the regulatory burden on generic manufacturers. The Act facilitated the generic production of patented drugs immediately upon the conclusion of the protected exclusivity period. However, it also allowed a patent holder to file an automatic injunction of 30 months against a generic competitor[30] to extend the duration of the patent when marketing was delayed by

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[24] JANET LUNDY, KAISER FAMILY FOUND., PRESCRIPTION DRUG TRENDS 3 (Sept. 2008), http://www.kff.org/rxdrugs/upload/3057_07.pdf (noting that the pharmaceutical industry has an excellent record of profitability from 1995-2007).

[25] Graham Dutfield, *The Pharmaceutical Industry, the Evolution of Patent Law and the Public Interest: A Brief History*, *in* EMERGING ISSUES IN INTELLECTUAL PROPERTY: TRADE, TECHNOLOGY AND MARKET FREEDOM 109, 136 (Guido Westkamp ed., 2007).

[26] *Id*. at 123.

[27] *Id*. at 141.

[28] Robert L. Ostergard, Jr., *Economic Growth and Intellectual Property Rights Protection: A Reassessment of the Conventional Wisdom*, *in* INTELLECTUAL PROPERTY, TRADE AND DEVELOPMENT: STRATEGIES TO OPTIMIZE ECONOMIC DEVELOPMENT IN A TRIPS-PLUS ERA 115, 155 (Daniel Gervais ed., 2007).

[29] *See* Gerald J. Mossinghoff & Vivian S. Kuo, *World Patent System Circa 20XX, A.D.*, 38 IDEA: J. L. & Tech. 529, 530-31, 549. (1998).

[30] 21 U.S.C.A. § 355(q)(1)(G) (2009).

regulatory hurdles.[31] The Hatch-Waxman Act appears to have been effective: nearly all top-selling drugs with an expired patent have generic versions, yet incentive among pharmaceutical companies to invent was not quelled in the least.[32] Meanwhile, few patent holders allow their pharmaceutical patent to lapse without restoring time lost in FDA approval.[33] The Hatch-Waxman Act expanded generic drug production—increasing availability of medications—but only by extending the exclusivity period of the patent holder.

Underlying the economic incentive mechanism of the patent system is the assumption that innovation will follow need and that market demand is an efficient manner by which limited resources may be properly allocated. For example, the modification of the patent system supported by the Hatch-Waxman Act assumes a patent holder wants to protect that property and that manufacturers are motivated to produce generic versions. This is an errant assumption. If profitable medicines are not necessarily ones that save the most, or any, human lives,[34] then, by contraposition, some medicines that save lives are not particularly profitable.[35]

For the most part, successful production of new medicines develops through business. Information assets, such as drug patents, have business relevance if there is a market relying on such assets related to a firm's business.[36] This is not a criticism of the profit motive of pharmaceutical companies as much a recognition that a firm is unlikely to invest where there is no market or the market is not relevant to the firm's core business. Data reported in PhRMA's annual report[37] reveal the relevant markets for pharmaceuticals: 91.8% of sales were made in the United States, Japan, Canada, and Western Europe.[38] Market-based incentives do not adequately encourage innovation to meet all public needs.

IV. EFFORTS TO BRIDGE THE GAP IN RESEARCH, DISTRIBUTION OF MEDICINES

Medical research has not adequately addressed the medical needs of developing

[31] 35 U.S.C.A. § 156 (a)(5)(2009).

[32] Thomas B. Leary, Comm'r, Fed. Trade Comm'n, Prepared Remarks at the Sixth Annual Health Care Antitrust Forum (Nov. 3, 2000) (transcript available at http://www.ftc.gov/speeches/leary/learypharma.shtm).

[33] NAT'L INST. FOR HEALTH CARE MGMT. FOUND., A PRIMER: GENERIC DRUGS, PATENTS AND THE PHARMACEUTICAL MARKETPLACE 4 (2002), http://www.nihcm.org/~nihcmor/pdf/GenericsPrimer.pdf

[34] Dutfield, *supra* note 25, at 119 ("Henry Gadsden, a head of Merck shortly after it had merged with Sharp and Dohme, told his researchers in a meeting that 'there are more well people than sick people. We should make products for people who are well.'").

[35] *See* AIDAN HOLLIS & THOMAS POGGE, THE HEALTH IMPACT FUND: MAKING MEDICINES ACCESSIBLE FOR ALL (2008), http://www.yale.edu/macmillan/igh/ (link to pdf document available here).

[36] CHRISTOPHER M. ARENA & EDUARDO M. CARRERAS, THE BUSINESS OF INTELLECTUAL PROPERTY 266 (2008).

[37] Of the pharmaceutical companies with the twenty highest revenues, all but two (Baxter International and Genentech) are members of PhRMA. *See* "Top 50 Pharmaceutical Companies Charts & Lists." 13 MED. AD. NEWS, Sept. 2007 at 1, 1; Pharm. Research & Mfrs. of Am. (PhRMA), Member Company List, http://www.phrma.org/about_phrma/member_company_list/members (last visited Oct. 14, 2008).

[38] PHARM. RESEARCH & MFRS. OF AM. (PhRMA), PHARMACEUTICAL INDUSTRY PROFILE 59 (2008), http://www.phrma.org/files/2008%20Profile.pdf.

countries.[39] When the needs of the developed world and the developing world align, the rigid protection of intellectual property restricts the sharing of knowledge at affordable prices and may lead the developing country to impose compulsory licensing.[40] Where medical needs do not overlap, the absence of a marketable customer base discourages innovation that may produce effective medical treatment. To put it bluntly, "companies direct their research where the money is, regardless of the relative value to society. The poor can't pay for drugs, so there is little research on their diseases, no matter what the overall costs."[41] The discussion below will examine the role that patent enforcement and non-patent methods could play in creating incentives for drug research for some of the neglected diseases of global health.

A. Stronger Enforcement of Intellectual Property Rights

In the context of patent incentives, one counter-intuitive explanation for the lack of innovation is heightened intellectual property rights. By protecting innovators from competition, intellectual property rights may discourage improvement of a patented drug therapy. Stiffer patent protections transfer value to the private holder at the expense of the public, even above the optimal value necessary to encourage innovation.[42] In other words:

> It is one thing to argue that the initial establishment of an IP institution generally encourages innovation, as opposed to a legal scenario that lacks any IP institutions. It is yet another to argue that the greater the defined scope of IP protection, the greater are the incentives for innovation.[43]

The point at which a private property right gives rise to innovation that meets a public need is a balance that must be found. Below the balance point, innovation will not be properly incentivized. Above that point the reward allocates resources less and less efficiently, resulting in deadweight loss.[44]

Conventional wisdom, manifest in the TRIPS agreement, has favored ever-increasing intellectual property protections. Under the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), the participating countries agreed that "patents shall be available for any inventions, whether products or processes, in all fields of technology."[45] Because this expansion of patent scope is a substantial shift for many countries, TRIPS protections do not cover that "which is necessary to protect *ordre public* or morality;" certain methods for the treatment of humans or animals; or plants

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[39] Global Forum for Health Research, *The 10/90 Report on Health Research 2003-2004*, xv, http://www.globalforumhealth.org/Site/003__The%2010%2090%20gap/001__Now.php.

[40] Robert Bird & Daniel R. Cahoy, *The Impact of Compulsory Licensing on Foreign Direct Investment: A Collective Bargaining Approach*, 45 AM. BUS. L.J. 283, 283-84 (2008).

[41] Joseph Stiglitz, *Prizes, Not Patents*, POST-AUTISTIC ECON. REV., May 18, 2007, at 46.

[42] Kenneth W. Dam, *The Economic Underpinnings of Patent Law*, 23 J. LEGAL STUD. 247, 257-61 (1994).

[43] DINA KALLAY, THE LAW AND ECONOMICS OF ANTITRUST AND INTELLECTUAL PROPERTY 49 (2004).

[44] Michael Abramowicz, *Perfecting Patent Prizes*, 56 VAND. L. REV. 115, 128-129 (2003).

[45] Agreement on Trade-Related Aspects of Intellectual Property Rights art. 27, Dec. 15, 1993, 33 I.L.M. 81 (1994).

and animals themselves.[46] Because of TRIPS, many low- and middle-income countries adjusted domestic patent law to broaden the scope of qualifying innovations.[47] "Normatively, TRIPS proponents argue that a uniform set of relatively high standards of protection fuels creativity and innovation, attracts foreign investment, and encourages a more rapid transfer of technology."[48] The shift presently benefits knowledge-based economies, but increased intellectual property rights are offered to developing countries as a necessary reform.[49]

Strengthening intellectual property rights may be a laudable goal, but some of the criticism of TRIPS has focused on the unintended consequences of this global shift. Keith Maskus has argued that in a global IP regime "what should matter is the ability of the domestic and international patent systems to support . . . firms' ability to compete in technology development and to protect their rights."[50] The emphasis is on enforcing existing patent rights, not expanding them. Broader rights "generate overlapping claims, monopoly power, and litigation costs that actually discourage competitive innovation."[51]

Maskus recommends that developed countries focus on enforcing existing intellectual property rights. Developed countries should "expand the global resources available for providing technical and financial assistance to . . . [developing] countries to improve their judicial systems and enforcement regimes."[52] While increased enforcement and stronger intellectual property protections are not mutually exclusive, innovation is better served by more reliable enforcement.[53] The establishment of minimum IP protections may be appropriate, but "harmonizing I[ntellectual] P[roperty] R[ights] to the highest possible standard, however, appear[s] to have an exclusionary effect, especially where capacity building necessary for the reception and embedding of technology in a developing economy is impaired."[54] Without the constraints of TRIPS or other agreements, a developing country's economic interest may be "to obtain IP as inexpensively as possible and grow their IP protection level in parallel with economic development and according to their own industrial and commercial strengths."[55] Indeed, the benefits of favoring stronger intellectual property protections "are most often

[46] *Id*.

[47] Ostergard, *supra* note 28, at 142.

[48] Laurence R. Helfer, *Regime Shifting: The TRIPS Agreement and New Dynamics of International Intellectual Property Lawmaking*, 29 YALE J. INT'L L. 1, 2 (2004).

[49] Jean R. Homere, *Intellectual Property, Trade and Development: A View from the United States*, *in* INTELLECTUAL PROPERTY, TRADE AND DEVELOPMENT: STRATEGIES TO OPTIMIZE ECONOMIC DEVELOPMENT IN A TRIPS-PLUS ERA 333, 338-340 (Daniel Gervais ed., 2007); *see also* Mossinghoff, *supra* note 30, at 538.

[50] KEITH E. MASKUS, COUNCIL ON FOREIGN RELATIONS SPECIAL REPORT NO. 19, REFORMING U.S. PATENT POLICY: GETTING THE INCENTIVES RIGHT 38 (2006).

[51] *Id*. at 5-6.

[52] *Id*. at 27.

[53] *Id*. at 38. For a perspective on increased intellectual property enforcement in the United States, see Prioritizing Resources and Organization for Intellectual Property Act of 2008, H.R. 4279, 108th Cong. (2008).

[54] Anselm Kamperman Sanders, *Intellectual Property Treaties and Development*, *in* INTELLECTUAL PROPERTY, TRADE AND DEVELOPMENT: STRATEGIES TO OPTIMIZE ECONOMIC DEVELOPMENT IN A TRIPS-PLUS ERA 157, 170 (Daniel Gervais ed., 2007).

[55] Ostergard, *supra* note 28, at 154.

characteristic of advanced, industrialized countries that do not face the specific issues that developing countries confront."[56]

As related to the transfer of intellectual property, the ratcheting up of intellectual property rights does not alleviate investment risks for the patent holder to the extent that increased enforcement could. China, which expanded the scope of its patent protections to become TRIPS-compliant,[57] provides an informative example. China has experienced a massive influx of technology despite its poor enforcement of patent laws because firms are willing to suffer the loss of intellectual property in order to "take advantage of the lower production costs and the emerging market."[58] The interest of pharmaceutical companies has been somewhat tempered by concern with protecting intellectual property.[59] Pharmaceutical companies have responded, however, by opening research and development centers within China, focusing on diseases relevant to the Chinese market and encouraging Chinese innovators through collaborative efforts.[60] Whether from foreign pressure or a domestic concern to protect native intellectual property, China has shown an increasing respect for intellectual property rights.[61] Increased enforcement of property rights is necessary to encourage patent owners to transfer their intellectual property, but enforcement will not encourage innovation absent a market incentive.

B. Patent Buyouts

Because the patent model has been so effective in stimulating innovation, the proponents of patent prizes and buyouts seek to augment the market-based incentives of patents to bridge the gap in innovation for neglected diseases. Though a market for drug therapies for neglected diseases does exist, the anticipated economic reward is insufficient to drive innovation. Under the prize system, governmental, international, or charitable organizations become market actors, injecting financial influence to support innovation. Advanced purchase agreements reliably funded by governments, for example, preserve economic incentive for patent holders.[62]

Determining a prize value sufficient to encourage innovation and ensuring that a reward is properly allocated depend on numerous factors. The perceived value of the

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[56] *Id*. at 129.

[57] Paroma Basu, *International Patent Law—Boon or Bane of Biotech?*, 23 NATURE BIOTECHNOLOGY 13, 15 (2005).

[58] Peter K. Yu, *Intellectual Property, Economic Development, and the China Puzzle*, *in* INTELLECTUAL PROPERTY, TRADE AND DEVELOPMENT: STRATEGIES TO OPTIMIZE ECONOMIC DEVELOPMENT IN A TRIPS-PLUS ERA 173, 180 (Daniel Gervais ed., 2007).

[59] Basu, *supra* note 57, at 15.

[60] VIVEK WADHWA ET AL., THE GLOBALIZATION OF INNOVATION: PHARMACEUTICALS: CAN INDIA AND CHINA CURE THE GLOBAL PHARMACEUTICAL MARKET? 11 (2008), *available at* http://www.kauffman.org/uploadedFiles/global_pharma_062008.pdf; *Novartis to Launch Strategic Biomedical R&D Center in Shanghai*, PHARMAMANUFACTURING.COM, Nov. 6, 2006, http://www.pharmamanufacturing.com/industrynews/2006/257.html.

[61] Maskus, *supra* note 50, at 25.

[62] Aidan Hollis, *Drugs for Neglected Diseases: New Incentives for Innovation*, *in* PHARMACEUTICAL INNOVATION: INCENTIVES, COMPETITION, AND COST-BENEFIT ANALYSIS IN INTERNATIONAL PERSPECTIVE 75, 82 (Frank A. Sloan & Chee-Ruey Hsieh eds., 2007).

innovation varies with the underlying product, the reliability of enforcement, the scope of including patent claims, and the length for which patent claims can be made.[63] Further, the reward – whether an expected market for a product or a patent prize – must be secure so that an innovator may have a reasonable expectation of recovering investment and making a profit. Joseph Stiglitz, 2001 Nobel Prize winner and former Chief Economist of the World Bank, points out that sharing knowledge has no additional associated cost so that "restricting knowledge is inefficient." Rephrasing Thomas Jefferson's recognition that knowledge property is not analogous to other forms of property, Stiglitz argues that the patent system incentive has left gaps in innovation that a patent prize could fill.[64] A prize would act on the market, reallocating "scarce research resources toward more efficient uses and ensuring that the benefits of that research reach the many people who are currently denied them."[65] There is tension between a moral imperative to provide life-saving treatments to those in need and using resources efficiently,

In a retrospective of patent rights during the industrial revolution, H.I. Dutton criticized efforts to establish prize systems to reward innovation because of their inability to properly allocate resources to a worthy invention or innovator: "Patents at least let the market decide."[66] Choosing a "winner" is a problem for current proposals as well, though the most attractive models integrate market success into a pricing mechanism.[67] One such proposal, a buy-out suggested by Kevin Outterson, would allow less desirable markets to obtain licensing rights from patent holders of existing drug therapies. Because "a robust level of research is assured by high-income markets alone,"[68] an incentive to innovate is assured. The licensing buy-out, paired with some assurance that generic manufacture will not bleed into other markets, will give some value to the patent holder without needing to compensate for the full cost of research and development. Thus, pharmaceutical firms would have an opportunity to expand distribution of drug therapies "to low-and medium-income countries without damaging patent rents from high-income countries."[69]

Using licensing agreements to further global health initiatives is a relatively new development. In the pharmaceutical industry, in particular, many variations of licensing agreements are commonly brokered to maximize value extracted from knowledge assets and products.[70] Outterson's proposal would identify a successful existing drug therapy that could be of use in the developing world, acquire a license limited to a geographic market, solicit generic manufacturing bids, and compensate the patent holder for the number of units sold at marginal cost with an agreed upon profit margin included.[71]

Currently, these licensing transfers do not exist because there is no profit to

[63] Maskus, *supra* note 50, at 9.
[64] Stiglitz, *supra* note 41, at 46.
[65] *Id*. at 47.
[66] H. I. DUTTON, THE PATENT SYSTEM AND INVENTIVE ACTIVITY DURING THE INDUSTRIAL REVOLUTION, 1750-1852, at 26 (1984).
[67] Hollis, *supra* note 62, at 82.
[68] Outterson, *supra* note 23, at 163.
[69] *Id*. at 164.
[70] ERIC M. DOBRUSIN & RONALD A. KRASNOW, INTELLECTUAL PROPERTY CULTURE 168 (2008).
[71] Outterson, *supra* note 23, at 171-173.

motivate the transfer. There is a close parallel found in the pharmaceutical business. Recently, Pfizer and Roche have effectively transferred geographic licensing—albeit under the designation of a partnership—to a company more willing to shoulder the risk of marketing a portfolio of drug products in Brazil and other developing economies.[72] Since the Brazilian government has sought to increase availability of low–priced drug therapies at the cost of intellectual property rights, large pharmaceutical companies have avoided the Brazilian market for fear of losing patent protection to compulsory licensing.[73] Stepping into the breach is moksha8, a firm backed by private equity investors.[74] Because a patent has value and the expansion of intellectual property has a non–rivalrous cost, drug patent holders may seek out alternative pricing arrangements to maximize the value of their property. For example, differential pricing schemes may grant low-income populations access to therapies at a lower price than high-income populations within the same country. While realizing marginal revenue is valuable, there is a concern of arbitrage as a low–priced product is offered to the high-price market and the difference is pocketed by a third party.[75]

From an economic perspective, the buy–out proposal is more effective at preserving the market reward of the patent holder than differential pricing or private licensing agreements. Unlike in a private licensing regime, the party buying out the patent is motivated to distribute the maximum number of generic units and the generic pricing undercuts the incentive for rival generic manufacturers to market the drug. Unlike under a differential pricing scheme, the market–wide use of generics would undercut the profit motive driving arbitrage. Any concern that customers who could otherwise afford drugs were taking advantage of the generic pricing could be shifted to the acquiring party. Indeed, if consumers in middle-income countries—namely, China, India and Brazil—would otherwise pay for the medicine, the "inequity is between the donor and the target country government," who "could compensate the donor for this inappropriate subsidy."[76] With increased enforcement efforts to restrict parallel importations, "[p]atented pharmaceuticals could be offered to more than 84% of the world's population at generic prices" without directly affecting patent rents.[77]

C. Patent Prizes

A patent prize is a mechanism that seeks to encourage innovation with the enticement of a reward; in other words, to "pull" research rather than "push" research

[72] *See moksha8 Launches Broad Product Portfolio in Key Emerging Markets*, REUTERS, Apr. 16, 2008, *available at* http://www.reuters.com/article/pressRelease/idUS160135+16-Apr-2008+PRN20080416.

[73] *See* Ricardo Amaral, *Brazil Breaks Patent on Merck AIDS Drug*, REUTERS, May 4, 2007, *available at* http://www.reuters.com/article/latestCrisis/idUSN04277757; *see also* Darren Schuettler, *Activists Hail Thai Move to Make Generic AIDS Drug*, REUTERS, Nov. 30, 2006, *available at* http://www.reuters.com/article/healthNews/idUSBKK5661020061130 (describing the appropriation of certain AIDS medications by the Thai government).

[74] *Drugs Companies and the Developing World – Quagmire to goldmine?*, ECONOMIST, May 15, 2008, at 77, *available at* http://www.economist.com/business/displayStory.cfm?story_id=11376895.

[75] *Id.* at 78.

[76] Outterson, *supra* note 23, at 172.

[77] *Id*. at 160.

through direct investment. In developed countries or where a market–incentive exists, a patent may sufficiently effect innovation. Without a market–incentive, an award or prize that acted "in such a way that the commercial incentives would be similar to those in high-income markets would be effective."[78] A typical patent prize proposal does not actually address neglected diseases at all, as much as it attempts to eliminate deadweight loss—or inefficiencies—present in the patent system. Indeed, "the risk and uncertainty" of a prize system may price the "loss" from the sale of a patent, while "the aggregate social value of projects is likely to be considerably greater than the total amount that the government offers."[79] A patent prize is most amenable to the pharmaceutical industry, where a single successful patent is closest to being a successful product.[80] The current patent system is itself a prize system, though the current "prize" is the "high prices and restricted access to the benefits that can be derived from the new knowledge."[81] Unlike a patent, a patent prize recognizes that a limited monopoly is an economic problem: not for fear of enriching the innovator but because the monopoly price discourages distribution.[82]

A prize may encourage innovation by making the patented knowledge part of the public domain—allowing other innovators the use of that knowledge—or by subsidizing the use of a particular product. Both of these outcomes are troubled, however, by the difficulties of both selecting prize–winners and determining the appropriate prize amount and delivery method to stimulate innovation.[83] As Michael Abramowicz's paper indicates,[84] success of a prize model system rests in the details of the proposal. The most ambitious prize proposal for neglected diseases would encourage pharmaceutical companies to bring a malaria vaccination to market by committing an aid organization to purchase doses as used.[85] On the surface, this proposal resolves the two main issues noted above: the prize "winner" is the party that administers a successful vaccine and the amount of the prize increases with each dose distributed. The amount committed for a successful program would be $3.1 billion, which would provide the private incentive to develop a malaria vaccine "yet still be extremely cost–effective from a public health perspective."[86] The basic concept to encourage innovation by guaranteeing a market is not a bad one, but reasonable criticisms of the effectiveness and sustainability of such a market exist.[87] More troubling, if the political and economic wills currently exist to

[78] Hollis, *supra* note 62, at 79.

[79] Abramowicz, *supra* note 44, at 126.

[80] *See* F. Scott Kieff, *Property Rights and Property Rules for Commercializing Inventions*, 85 MINN. L. REV. 697, 707-710 (2000).

[81] Stiglitz, *supra* note 41, at 47.

[82] Abramowicz, *supra* note 44, at 128.

[83] *See id*. at 235.

[84] *Id*. at 121.

[85] Ernst R. Berndt et al., *Advanced Purchase Commitments for a Malaria Vaccine: Estimating Costs and Effectiveness* 3, 23 (Nat'l Bureau of Econ. Research, Working Paper No. 11288, 2005).

[86] *Advanced Purchase Commitments for a Malaria Vaccine*, 12 NAT'L BUREAU OF ECON. RESEARCH: BULLETIN ON AGING AND HEALTH 1, 2 (2005), *available at* http://www.nber.org/aginghealth/summer05/summer05.pdf; *see also* ADVANCE MARKET COMMITMENT WORKING GROUP, CTR. FOR GLOBAL DEV., MAKING MARKETS FOR VACCINES: IDEAS TO ACTION (2005), *available at* http://www.cgdev.org/section/initiatives/_archive/vaccinedevelopment/chapters (follow hyperlinks to consecutively paginated chapter pdf files).

[87] Donald W. Light, *Making Practical Markets for Vaccines*, 2 PLOS MED. e271 (2005), *available at* http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0020271.

encourage new vaccinations for malaria, why is there no money available to increase the distribution of effective existing treatments for infectious diseases?[88]

V. A COST-SHIFTING MECHANISM: PRIORITY REVIEW VOUCHERS

A. From Proposal to Law

On September 27, 2007, President George W. Bush signed into law House Resolution 3580, more readily known as the Food and Drug Administration Amendments Act of 2007 (FDAAA).[89] Among the numerous statutory changes and amendments made in the act was section 1102, which added section 524 to the Food, Drug, and Cosmetic Act.[90] Section 524 authorizes the "FDA to award priority review vouchers to sponsors of certain tropical disease product applications that meet the criteria specified by the Act."[91] Relevant to the market incentive discussion above, a qualifying applicant will receive a transferable priority review voucher that may be used or sold for use with a second treatment relating to human drug research.

The political initiative for the priority review voucher arose from a presentation by members of U.S. Sen. Sam Brownback's (R-Kansas) staff and an article published by the same presenters, Duke University economists David Ridley, Henry Grabowski, and Jeffrey Moe.[92] Sen. Brownback was interested because the incentive proposed in the Duke article "avoids the political divisiveness of pharmaceutical patent extensions."[93] Indeed, later guidance by the FDA provides politically palatable reasons to incentivize treatment for tropical diseases: "intercontinental jet transport, immigration, tourism, and military operations are increasing the direct impact these diseases have on the health of Americans."[94]

The voucher system, as proposed in the original paper by Ridley, Grabowski and Moe, is presented within the context of other push and pull mechanisms that can be used to stimulate innovation. Other mechanisms discussed include the Orphan Drug Act, public-private partnerships (PPPs), and Advanced Market Commitment, although these

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[88] *See* Andrew Farlow, The Cost of R&D: How Much Money Is Needed to Address the Current Need?, Presentation to the International Conference on Ensuring Innovation for Neglected Diseases (June 8, 2005) (PowerPoint file at http://www.economics.ox.ac.uk/members/andrew.farlow/ under title of presentation).

[89] Press Release, White House, President Bush Signs H.R. 2669 and H.R. 3580 into Law (Sept. 27, 2007), *available at* http://georgewbush-whitehouse.archives.gov/news/releases/2007/09/20070927-5.html.

[90] Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, 121 Stat. 972 (to be codified at 21 U.S.C. § 360n).

[91] CTR. FOR DRUG EVALUATION & RESEARCH (CDER) & CTR. FOR BIOLOGICS EVALUATION & RESEARCH (CBER), FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: TROPICAL DISEASE PRIORITY REVIEW VOUCHERS (2008), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM080599.pdf (non-binding, for comment purposes only).

[92] Sen. Sam Brownback, *Eliminating Neglected Diseases: Impact of Published Paper*, 26 HEALTH AFF.1509, 1509 (2007).

[93] *Id.*

[94] CDER & CBER, *supra* note 91, at lines 41-42; *see* David Brown, *Man with Rare TB Detained, Isolated; He Ignored Orders, Traveled Extensively*, WASH. POST, May 30, 2007, at A03.

methods are arguably targeted at high-profile diseases such as malaria and HIV/AIDS, not lesser-known diseases such as leishmaniasis and trypanosomiasis.[95] The underlying function of each method is to align an economic incentive—so ably employed by patent law—with a purpose that does not intrinsically have any financial pull.

In the past, patent extensions were proposed as a carrot to patent holders for granting generics access to clinical studies–notably in the Hatch-Waxman Act–but they were also proposed as a mechanism to drive innovation, though with less success.[96] Whereas the extension of pharmaceutical patents—the so called "wildcard patent provision" of the Project BioShield Bill, [97] rejected in 2005—limited rewards for innovation to those companies that possessed existing valuable patents and played havoc with generic manufacturers, a priority review voucher is of value to any innovator as they then have the option of using or selling the voucher.

Ridley, Grabowski and Moe note that a successful voucher will create value for the drug producer, the voucher purchaser and for global welfare.[98] Obviously, the priority review voucher has the potential to reduce bureaucratic delay for a non-qualifying human drug treatment, effectively extending the marketable patent term from the beginning of a drug's marketing life instead of the end. Henry Grabowski, a co-author on the original article, speculated that the voucher "could be worth $300 million to a biotech or pharmaceutical firm" or even "$1 billion or more for some companies if their products achieve blockbuster status."[99] The actual sale price for a voucher will depend on a variety of factors, the least of which being supply and demand. For the producer, total value is the sum of the voucher use or sale, along with Orphan Drug Act tax credits and goodwill.[100] Finally, the social value of having a treatment for a neglected disease is compounded by expedited access to a blockbuster drug in developed economies.[101] Interestingly, the same disjunction between economic and social value that requires non-patent mechanisms to bridge the gap in incentives also allows for the possibility that a priority review voucher could work.

B. The Priority Review Voucher in Law

Section 524 became law on Sept. 27, 2007 when President Bush signed Pub. L. No. 110-85, 121 Stat. 972 (to be codified at 21 U.S.C. § 360n). The law authorizes the FDA to confer a transferable priority review voucher to a sponsor of an infectious disease

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[95] David B. Ridley, Henry G. Grabowski & Jeffrey L. Moe, *Developing Drugs for Developing Countries*, 25 HEALTH AFF. 313, 316-17 (2006).

[96] *See* Biological, Chemical, and Radiological Weapons Countermeasures Research Act, S. 666, 108th Cong. (2003).

[97] Marc Kaufman, *Bioterrorism Response Hampered by Problem of Profit*, WASH. POST, Aug. 7, 2005, at A05.

[98] Ridley, *supra* note 95, at 318-19.

[99] Donna Young, *Priority Review Vouchers: the Next 'Golden Ticket'?*, 19 BIOWORLD TODAY Issue 49, Mar. 12, 2008, *available at* http://www.bioworld.com/servlet/com.accumedia.web.Dispatcher?next=bioWorldHeadlines_article&forceid=47070.

[100] Ridley, *supra* note 95, at 319.

[101] *See id.* at 318.

treatment upon approval of the primary application by the FDA.[102] The priority review voucher entitles the user to the FDA's review and action "not later than 6 months" after applying.[103] Current estimates for a standard review vary from 10 to 18.4 months,[104] so an expedited review would reduce the regulatory waiting period at the beginning of a drug's marketing life at least four months and as much as an entire year. The FDA will recoup some of the costs associated with its priority review burden by collecting fees from applicants—currently $1,178,000—and it will also require that applicants give one year's notice.[105] While there is no current evidence to indicate that a priority review is less safe than a standard review,[106] there is some evidence to suggest that withdrawals and new "black-box warnings" occur at a higher rate among FDA approvals subject to a deadline than among approvals not subject to a deadline.[107]

The primary tropical diseases include tuberculosis, malaria, and cholera, but it is also noted that the Secretary may designate "[a]ny other infectious disease for which there is no significant market in developed nations and that disproportionately affects poor and marginalized populations."[108] As Kevin Outterson notes, chronic global diseases have impacted developing countries as well as developed countries.[109] Here, legislation limits applicant sponsors to "tropical" and "infectious" diseases only because—as the FDA's guidance indicates—"existing incentives have been insufficient to encourage development of new and innovative drug therapies" for qualifying diseases.[110] In line with this reasoning, drugs that qualify for FDA approval under 505(b)(2)—existing patents either expired or asserted to be invalid—or 505(j)—abbreviated new drug applications—do not qualify for the voucher.[111]

Under the new law, combination drugs with an active ingredient previously approved as a drug for human use do not qualify for a priority review voucher.[112] From this requirement it is apparent that a new chemical entity (NCE) is sought, but it is worth noting that there are no limitations to exclude existing non-FDA treatments. Under the FDA guidance, "products eligible that have been approved and used in other countries but have not previously been submitted for review by the FDA" may qualify as long as they meet the criteria other applications must meet under 21 U.S.C.A. § 360n (a)(4).[113]

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[102] 21 U.S.C.A. § 360n(b)(1) (2009).

[103] *Id.* § 360n(a)(1).

[104] CDER & CBER, *supra* note 91, at line 159; Ridley, *supra* note 95, at 318.

[105] 21 U.S.C.A. § 360n(b)(4), (c) (2009); Henry Grabowski, David B. Ridley, Jeffrey L. Moe, *Priority Review Vouchers to Encourage Innovation for Neglected Diseases* (Sept. 2008) (unpublished manuscript, *available at* http://www.law.harvard.edu/programs/petrie-flom/workshops_conferences/2008_workshops/Grabowski.pdf).

[106] Ridley, *supra* note 95, at 322.

[107] Keith J. Winstein, *Late Drug Approval Linked to Safety Issues*, WALL ST. J., Mar. 27, 2008, at D1, *available at* http://online.wsj.com/article/SB120656190873766273.html?mod=todays_us_personal_journal. *But see* FOOD AND DRUG ADMIN., FDA DATA ON PDUFA DRUG APPROVALS (2008), *available at* http://www.fda.gov/oc/pdufa/FDADrugAppSafetyData_files/NMESafetySumm.html.

[108] 21 U.S.C.A. § 360n(a)(3).

[109] Outterson, *supra* note 23, at 161, 173.

[110] CDER & CBER, *supra* note 91, at lines 38-40.

[111] Young, *supra* note 99.

[112] 21 U.S.C.A. § 360n(a)(4)(C) (2009).

[113] CDER & CBER, *supra* note 91, at lines 267-271.

The priority review voucher seeks to stimulate innovation, but there is no requirement "to market or distribute the qualifying tropical disease product after approval."[114] At first glance, granting a priority review voucher before the treatment is marketed or otherwise developed seems to defeat the purpose of the innovation. While it is unlikely that a developer would create a qualifying treatment for the voucher alone, there is value for the treatment beyond the value of the voucher. Depending on the prevalent voucher market and the tax breaks available from the Orphan Drug Act, a developer may create the treatment at a substantially greater cost than the market value of the product. Given the invested value, the remaining intellectual property rights have some value that the innovator could extract. Because this patent value is not the core economic recovery model for the innovator, an innovator may be amenable to a patent buyout or regional licensing in order to extract the remaining value from the innovation. Allowing transferability of the vouchers and limiting the commitment of the innovators are the most significant features of the voucher program.

C. Pushback and Criticisms

Since the priority review voucher program became law, there have been many questions and a few published criticisms of the program. First and foremost, the FDA issued a guidance document in October 2008 to address many questions about the administration and technical requirements of the voucher program. This document restated the purpose of the amendment and answered several commonly asked questions. The FDA acts on 90% of priority review applicants within six months, but a voucher will not guarantee that deadline; a drug already approved for another indication does not qualify for the voucher; and qualifying drugs may also meet the criteria of the Orphan Drug Act.[115]

The purpose of the vouchers is to stimulate innovation for the treatment of neglected tropical diseases, but many large pharmaceutical companies—those who may pay and benefit most from the priority review vouchers—are skeptical of the process and are hesitant to participate until the system is better understood. Research has shown that the pharmaceutical industry is wary of the credibility of the program and unsure how to allocate research given the speculative value of a voucher.[116] Of greatest concern is how the FDA will fit a standard application into a priority review voucher slot. As noted above, the FDA guidance allows that 90% of priority reviews will be completed within six months. However, because the industry believes the FDA tolerates higher risk for a medically necessary drug, the FDA is more likely to extend a priority review to standard review than allow a non-medically necessary drug a higher risk tolerance.[117] Compounding the problem is the fact that "sponsors will want to use the vouchers in precisely the markets where FDA is most likely to complete a review by asking for more

[114] *Id.* at lines 175-179.

[115] *Id.* at lines 241-244, 248, 273-276, 303-305.

[116] *See* Grabowski, *supra* note 105, at 8-9; McCaughan, *supra* note 7, at 2 ("As Wyeth SVP-corporate business development Thomas Hofstaetter puts it: 'I would need to see the first example before I really believe it.'").

[117] McCaughan, *supra* note 7, at 2.

data."[118] In other words, the actions of the FDA in how it handles the priority review vouchers will help shape the success of the tropical disease incentive program.

The value of the priority review voucher is truly unknown, but there are several factors to consider. One factor is timing. Pharmaceutical companies would need to decide upon a review of Phase III data – on efficacy and safety of the drug for human use – whether to pursue or use a priority review voucher and at what price. While a mature and successful drug such as Lipitor may earn as much as $2.5 billion in four months, it is unlikely that even the most optimistic development manager would have such lofty expectations prior to FDA approval.[119] There will be a discrepancy between the price paid for a voucher and the potential value gained by the purchaser. Another significant factor in the value of the voucher will be the number of vouchers on the market at a given time and the amount of demand. Companies with a developed drug pipeline have timing expectations that cannot easily be altered to meet the market availability of a voucher. That being said, vouchers do not expire and may be held or transferred as an asset in anticipation of heightened demand or deep pockets in the marketplace.

Criticisms outside the pharmaceutical industry focus on the failure to require dissemination of the innovation.[120] The recipient could license or otherwise share the approved—and, presumably patented—drug therapy, but the priority review voucher is not contingent on the recipient doing so. One critic favors the auctioning of priority review vouchers with proceeds to be granted as prizes.[121] Unlike a prize, in which a donor chooses the winner, funds the project, and hopes for success, the voucher rewards the innovative efforts that gain FDA approval. True, the problem of distribution remains, but a rational actor would extract value from the remaining intellectual property by either licensing or selling the property.[122]

A more focused critique questions the effectiveness of the mechanism itself. First, the incentive is distinct from the innovation it seeks to stimulate.[123] Large drug companies are unlikely to shift their research resources to account for the uncertain value of a priority review voucher, and small companies that do so are unlikely to have an individual need for the voucher.[124] Pharmaceutical companies have noted that there is value in the voucher, but how much is unknown. Second, the voucher legislation does not specify the quality of the treatment, although it does categorically reject combination treatments that may provide significant improvements to treatment. While effective combination treatments do not qualify for the voucher, the tropical disease treatment must qualify for priority review itself. To do so an application must meet Center for Drug Evaluation and Research's requirement that it is (1) safe and effective where no

[118] *Id*. at 7.
[119] *Id*. at 8.
[120] Knowledge Ecology International, *supra* note 4.
[121] *Id*.
[122] ARENA & CARRERAS, *supra* note 36, at 242.
[123] Aaron S. Kesselheim, *Drug Development for Neglected Diseases—The Trouble with FDA Review Vouchers*, 359 NEW ENG. J. MED. 1981 (2008).
[124] *Id*.

alternative exists or (2) a significant improvement compared to marketed products.[125] Third, there is no requirement to distribute the approved drug therapy. Perhaps it is a weakness of the legislation not to encourage distribution; but to require an innovator to do so or to link benefits to low-cost access would discourage innovators from seeking a priority review voucher. Fourth, applying pressure to the priority review system might result in poor regulatory work. However, the FDA seems more likely to maintain strict safety standards, frustrating the expedited timeline first. In place of a voucher system, Kesselheim recommends a prize system akin to an Advanced Market Commitment (AMC) or a non-profit/government development that allows for licensed distribution. These initiatives are gaining momentum, but they too are in their infancy[126] and are at risk of the fallibility of patent prizes: picking winners poorly or misallocating resources in the process.

VI. CONCLUSION

The patent system functions because a successful patent seeker can rely on the right of market exclusivity to reap the rewards of the invention protected. A patent is flawed in that its value is created by transferring knowledge that is otherwise restricted: the indignity of a limited monopoly that the public suffers to gain innovation from private ingenuity. For present purposes, the patent system is flawed because there are gaps where market demand is too weak to drive innovation and a public need goes unmet. In leaving the patent system however, we leave the settled expectations upon which innovators rely and use to make decisions on resources invested.

Global health initiatives have become more sophisticated and collaboration has become a hallmark of recent successful global health strategies. Because there are many interested participants, there are many proposals on how to best administer global efforts and resources. The most frequent criticisms against priority review vouchers and Advance Market Commitments are that they misallocate resources better used in the distribution of existing treatments, and not as an incentive for future treatments.

Optimal social utility of innovation and access to treatments for neglected diseases can only be approached piecemeal. Where a patent buyout may encourage a patent holder to license pharmaceuticals for a narrow geographic designation, the parallel importation of generics undermines the incentive to license and risk real loss in other markets. Reliable intellectual property rights enforcement is necessary. Where no incentive exists for innovation and tropical diseases have no recognizable treatment, a buyout will serve no purpose. Incentives are necessary to stimulate innovation for neglected diseases. Where an innovator has successfully navigated a patent thicket and developed a treatment of a neglected disease, there is no social utility gained until it is implemented and reaches the intended population.

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[125] Manual from Dir., Office of New Drugs, Center for Drug Evaluation & Research, MANUAL OF POLICIES AND PROCEDURES 6020.3 1-2 (July 16, 2007), available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/StaffPoliciesandProcedures/ucm082000.pdf.

[126] *See* Grabowski, *supra* note 105.

There is no single correct method that will result in increased prevention and treatment of neglected diseases in the developing world. In fact, a combination of proposals would buttress the weaknesses of any one approach. From innovation, to knowledge transfer, to distribution of needed treatments, the steps that lead to improved world health are connected. It is important to recognize that no single approach however, can—or should try—to cover every step from the laboratory to the clinic.