Pharmaceutical Arbitrage

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Kevin Outterson[1]

I. Introduction

Expensive prescription drugs lie at the heart of two major public health issues: the AIDS epidemic in sub-Saharan Africa; and US patients obtaining less expensive drugs from Canada over the internet. Both situations call for reducing financial barriers to innovative drugs while maintaining incentives to promote innovation. The WTO TRIPS Agreement on intellectual property is the global nexus for these issues.[2]

Health care policymakers frequently grapple with providing access at reasonable cost while improving quality. Cost, quality, and access figure prominently in debates over pharmaceutical pricing.[3] Prices are high, economists say, because pharmaceutical innovation is expensive. The research and development (R&D) enterprise must be nurtured, creating the next generation of break-through therapies.

Other voices counter that without financial access, innovation is a cruel taunt. New wonder drugs won't improve health unless patients actually get them. Pharmaceuticals, it is argued, are not normal market goods to be distributed primarily to the wealthy. Advocates claim special status for health care goods and services, frequently bolstered

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[1] Associate professor of law, West Virginia University College of Law. Comments and questions to Kevin.Outterson@mail.wvu.edu. Special thanks to the American Society of Law, Medicine & Ethics 2003 Health Law Young Scholars Workshop and the College of Law Faculty Workshop for helpful comments and suggestions. This research was supported by a Hodges Research Grant from the West Virginia College of Law. An early draft of this article was prepared during my tenure as a Visiting Fellow at the Lauterpacht Research Centre for International Law at the University of Cambridge. I thank the Centre and its people for their hospitality.

[2] Agreement on Trade-Related Aspects of Intellectual Property Rights, Annex 1C of the Marrakesh Agreement Establishing the World Trade Organization, Apr. 15, 1994, 1869 U.N.T.S. 299, art. 1, § 1 [hereinafter TRIPS or TRIPS Agreement]. The US implemented the WTO agreements in the Uruguay Round Agreements Act, Pub. L. No. 103-465, 108 Stat. 4809 (1994).

[3] Most participants in these debates recognize the need for balancing cost, quality and access. *See, e.g.,* Carlos M. Correa, *Implications of the Doha Declaration on the TRIPS Agreement and Public Health* 7-9, WHO Doc. WHO/EDM/Par/2002.3 (June 2002) [hereinafter Correa, *Implications of Doha*].

with appeals to human rights. Innovation and quality must be balanced with access and cost.

Differential pricing is the pharmaceutical industry's preferred solution to inadequate financial access to anti-retroviral (ARV) therapies for AIDS. Differential pricing permits drugs to be sold cheaply in low-income countries, while maintaining high prices in markets like the United States.[4] Unfortunately, this 'solution' to the AIDS crisis creates the demand for cheap drugs from Canada: Americans increasingly resist paying the highest global prices for patented drugs. Differential pricing is under siege as Americans turn to Canada and other nations for cheaper patented drugs. In both situations, pharmaceutical arbitrage plays the central role.

This article explores the key functions of pharmaceutical arbitrage, its impact on the cost-quality-access dynamic, and implications for the TRIPS Agreement and related government interventions. Part One establishes a theoretical framework for understanding pharmaceutical markets and innovation, utilizing the heuristic device of *optimal patent rents*. Part Two applies this framework against two case studies on ARV pricing in sub-Saharan Africa and Canadian-US pharmaceutical arbitrage.

The primary conclusions are encouraging: the benefits and the burdens of innovation can be shared equitably. Optimal incentives for innovation can be maintained while providing greatly expanded essential medicines access to the poor. The Doha Declaration at the WTO Ministerial Conference,[5] and the subsequent Cancun modifications to TRIPS[6] did not hinder innovation. Going forward, the Doha agenda can safely expand to many disease categories beyond AIDS, tuberculosis, and malaria, without undermining innovation. Modifications to TRIPS should also implement a 'reference licensure' system and a compulsory licensure process. Preventing pharmaceutical arbitrage from low-income markets into high-income markets is the linchpin to this analysis.

However, other forms of pharmaceutical arbitrage should be encouraged, as they deliver lower prices to consumers and may assist in resolving global free rider problems in pharmaceutical pricing. Arbitrage within and between high-income countries, such as the Canadian internet sales to the US, satisfies this condition. Innovation does not require restrictions on parallel trade within and between high-income countries or between or to low-income countries. Moreover, effective differential pricing requires the credible threat of compulsory licensure, and this process should be streamlined.

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[4] *See* World Health Organization, Report of the Workshop on Differential Pricing and Financing of Essential Drugs: A WHO/WTO Secretariat Workshop (2001) *available at* http://whqlibdoc.who.int/hq/2001/a73725.pdf (the WHO WHOLIS library); *see generally* Brigitte Granville, ed., The Economics of Essential Medicines (2002).

[5] World Trade Organization, Doha Declaration on the TRIPS Agreement and Public Health, WT/MIN(01)/Dec/2 (Nov. 20, 2001) [hereinafter Doha Declaration].

[6] World Trade Organization, Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health, WT/L/540 (Decision of the General Council of 30 August 2003) [hereinafter Cancun Provisional Waiver].

Several global market failures in pharmaceutical markets and innovation are also addressed, particularly for neglected disease conditions such as malaria. Several commentators have argued that strong intellectual property (IP) rights in developing nations are required in order to stimulate development of neglected disease drugs. This claim is thoroughly refuted, with major implications for TRIPS implementation. In particular, a virtual IP rights regime is proposed, combined with binding purchase commitments by donors. Other conclusions entail streamlining national drug regulatory systems, and improving designs for subsidies and price controls.

Finally, some pharmaceutical innovations are exhaustible and require special consideration. Antibiotics are a paradigm case: by the time the patent expires, the antibiotic may be worthless due to bacterial resistance. While some have argued for longer or perpetual patent terms for exhaustible patented pharmaceutical, this proposal is incompatible with differential pricing for the poor. Another solution is proposed here, involving a binding purchase commitment by a donor followed by rationing through evidence-based medicine.

PART ONE. THE THEORY OF PHARMACEUTICAL ARBITRAGE

II. Differential Pricing and Pharmaceutical Arbitrage

A. Differential Pricing

In the neoclassical economic model, goods are sold at a single market-clearing price. Clever selling firms realize that some customers will pay more than the market-clearing price. The selling firm increases its profit by selling each item at the highest price each particular buyer will pay. The economic literature identifies this process as *price discrimination*, which is synonymous with differential pricing for our purposes.[7] Differential pricing is common. The same product is frequently sold at different net prices to various buyers.[8] The seller segments the markets for its product, and charges what each market segment will bear. The airline industry provides a common example. On almost every flight, passengers will have paid many different prices for the same service.[9] The market has been segmented into multiple buyer groups, including business travelers, vacation travelers, frequent flyers, and last minute purchasers.[10]

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[7] *Price discrimination* is the term generally utilized in the economic literature, but should not be confused with price discrimination under the Robinson-Patman Act, 15 U.S.C. §§13-13b, 21a (2004). This article follows the usage most common in the essential medicines literature, *differential pricing*. Tiered pricing and price segmentation are other terms occasionally used for pharmaceutical differential pricing. *See, e.g.,* DG Trade, European Union, Tiered Pricing for Medicines Exported to Developing Countries, Measures to Prevent Their Re-Importation into the EC Market and Tariffs in Developing Countries (EU Working Document, Apr. 22, 2002).

[8] This particular definition is found in Louis Philips, The Economics of Price Discrimination 6, 17 (1983).

[9] A charter flight might be an exception if everyone on board paid the same price, but then the charter flight itself is a form of market segmentation and differential pricing.

[10] Louis Philips argues that the airline example is not technically an example of price discrimination, concluding that reserving a seat weeks in advance and buying a last minute ticket are different services.

Given great variation between buyers, a selling firm might attempt to differentiate its prices on an individual sale basis, a pure form of differential pricing which Pigou labeled *first-degree price discrimination.*[11] First-degree price discrimination is also known as *perfect price discrimination*, since it fully extracts all consumer surplus for the benefit of the producer.[12]

Transaction costs almost always make first-degree differential pricing untenable: the marginal costs of collecting and understanding all of the relevant factors for each buyer usually outweigh the gains in marginal revenue.[13] If the number of market segments is kept relatively small, however, the marginal revenue may exceed the marginal cost, resulting in *second- or third-degree price discrimination.*[14] In second-degree price discrimination, purchasers segment themselves into price levels. For example, railroad passengers choose either first, second or third class seats. In third-degree price discrimination, the producer segments the market, generally using monopolistic power to distinguish the different prices customers are willing to pay. Global sales of patented pharmaceuticals are a prime example of third-degree price discrimination. The focus of this article is third-degree price discrimination, but the term *differential pricing* will be used, following the established usage in the essential medicines literature.[15]

B. Arbitrage

Arbitrage is the nemesis of differential pricing.[16] Differential pricing assumes that the first purchaser is the ultimate user. Delta Air Lines is willing to sell some seats cheaply to vacationers so long as it is certain that only the vacation buyers are being satisfied at rock-bottom prices. The Saturday night stay requirement is commonly imposed to distinguish between business and vacation travelers for differential pricing purposes.

Arbitrage occurs when buyers in a lower-priced market re-sell the product to consumers in a higher-priced market. Pharmaceuticals sold for $5 in India may be identical to products sold for $1000 in the United States, creating the opportunity for arbitrage or parallel trade.[17] Absent other constraints, arbitrage will erode price-differentiated

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Philips, *supra* note 8, at 9. Nevertheless, the example is ubiquitous and easily grasped. *See, e.g.,* Ernst R. Berndt, American Enterprise Institute for Public Policy Research, Uniform Pharmaceutical Pricing: An Economic Analysis 5-6, 9-10 (1994).

[11] The classic description of first-, second-, and third-degree price discrimination is found in Pigou, The Economics of Welfare ch. 17 (4th ed. 1920). A helpful summary of Pigouvian price discrimination may be found in Philips, *supra* note 8, at 11-14.

[12] Philips, *supra* note 8, at 158.

[13] Pigou, *supra* note 11, at 280.

[14] *See* Pigou, *supra* note 11; and Philips, *supra* note 8, at 12-13.

[15] *See, e.g.,* Granville, *supra* note 4.

[16] For a thorough discussion of the interplay between arbitrage and differential pricing, *see* Philips, *supra* note 8, at 14-16.

[17] When pharmaceutical arbitrage crosses a political frontier, it is called *parallel trade:* "also called grey-market trade, is the act of taking goods placed into circulation in one market, where they are protected by a trademark, patent or copyright, and shipping them to a second market without the authorization of the local owner of the intellectual property right." Keith E. Maskus & Mattias Ganslandt, *Parallel Trade in*

markets, moving all sales towards an equilibrium price. As a result, arbitrage redirects consumer surplus away from the producer, and into the hands of the consumer.[18] This is generally considered to be a good thing, leaving more money in the hands of consumers.

C. The Law and Economics of Pharmaceutical Arbitrage

Successful price discriminators must minimize arbitrage by customers. Several tactics may be deployed, including contracts, product differentiation, and regulatory structures. Each tactic is a pressure point for pharmaceutical arbitrage, as well as a potential policy tool.

1. Contract

Private ordering may support differential pricing. The contract between buyer and seller may forbid arbitrage. Airlines generally forbid the transfer of tickets. Firms may contractually prohibit parallel trade of their products. If a buyer breaches the agreement, the seller can pursue contractual remedies to punish arbitrage. Some firms refuse to sell equipment, but only lease it with sub-leasing forbidden.[19]

The effectiveness of contractual remedies will depend upon whether the seller has privity with every arbitrageur, and in the monitoring costs required to ensure compliance. In pharmaceutical arbitrage, multiple layers of pharmaceutical distributors and retailers lack privity.[20] Contractual approaches may also run afoul of competition law. The European Court of Justice has struck down some contractual provisions preventing intra-European arbitrage as anticompetitive.[21]

2. Product Differentiation

Arbitrage requires a substitutable product. If the product is fungible and movable, then the consumer can easily collapse the price discriminating market segments.[22] Producers rarely concede strict fungibility: product differentiation and marketing are deployed to support differential pricing. Aspirin might be considered a fungible commodity. The active ingredient is well known and unprotected by patents. And yet the aspirin market is filled with differentiated products. Some aspirins are marketed with brand names as proxies for safety and reliability. Others are compounded with other ingredients such as

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Pharmaceutical Products: Implications for Procuring Medicines for Poor Countries, in The Economics of Essential Medicines 57 (Brigitte Granville, ed., 2002). The practice is not necessarily illegal, depending upon the country's laws concerning exhaustion of IP rights. *See infra* Section II.C.3.b.

[18] Philips, *supra* note 8, at 18.

[19] The famous example of Xerox is described in Philips, *supra* note 8, at 151-153.

[20] Another form of arbitrage suppression through contract is the use of uniform delivered prices for bulky products. Philips, *supra* note 8, at 23-30. This is probably not present in consumer drug markets due to the high value to weight ratio.

[21] Case C-306/96, Javico International and Javico AG v. Yves Saint Laurent Parfums SA, 1998 E.C.R. I-1983, [1998] 5 C.M.L.R. 172 (1998).

[22] Berndt, *supra* note 10, at 8-10. Philips, *supra* note 8, at ch. 1.

caffeine or buffering agents. Aspirin may be purchased in particular sizes, shapes and delivery methods such as pills, capsules, or gel caps. Despite this product differentiation, at some level all aspirins are subject to substitution. If the preferred brand or form of aspirin is unavailable, or priced too high, some consumers will substitute another form of aspirin, or may even substitute with another class of analgesic such as ibuprofen or acetaminophen.

Transaction costs influence the ease of substitution. If transaction costs are low, products may be easily compared and found to be substitutable. Conversely, high transaction costs inhibit substitution. Differential pricing is easier to sustain to the extent the product is less substitutable and to the degree that transaction costs are relatively high.

3. Government Intervention

Regulatory structures influence substitution, transaction costs, and arbitrage. Government is not a neutral bystander, but generally blocks pharmaceutical arbitrage across political borders, without appropriately balancing the health policy goals of cost, quality and access. Two major categories are examined: drug regulatory agencies (DRAs) and intellectual property (IP) laws.

a. Drug Regulatory Agencies (DRAs)

DRAs support differential pricing on a country by country basis. The approval process for patented and generic drugs is left to individual countries under the TRIPS Agreement.[23] In the United States, the DRA is the Food and Drug Administration (FDA). The FDA regulates drug approval and marketing, important factors in creating and sustaining differential pricing.

In 1997, the FDA modified its regulations to permit direct to consumer (DTC) advertising for pharmaceutical drugs.[24] Drug companies have responded to this opportunity by deploying vast resources to market prescription drugs, exceeding $2.5 billion by 2000.[25] DTC advertising encourages substitution of the advertised drug in place of competitors' drugs, while discouraging substitution in the other direction. The modification of the DTC rule by the FDA thus creates opportunities for substitution and arbitrage, by

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[23] TRIPS, *supra* note 2, at art. 1, § 1.

[24] The regulations are now found at 21 C.F.R. § 202.1 (2004). As of 2000, only the US and New Zealand permitted DTC ads. NIHCM Foundation, Prescription Drugs and Mass Media Advertising 16 (2000). In 2002, Canada also permits restricted DTC advertising, and is affected by spillover from American media. Canadian Institute for Health Information, Drug Expenditure in Canada: 1985-2002 41 (2003) (also describing how spillover of American DTC advertising increases utilization in Canada).

[25] NIHCM Foundation, *supra* note 24, at 2. Spending for DTC advertising grew at an annual rate of 44.9% from 1995 to 2000, and is now growing at an annual rate of 9.4% thereafter. Stephen Heffler, et al., *Health Spending Projections For 2002-2012,* Health Affairs (Web Exclusive, Feb. 7, 2003) *available at* http://www.healthaffairs.org, at nn. 24-26 and text accompanying. Product shift, increased unit prices, and increased volumes each account for about a third of the growth in prescription drug spending. C. Daniel Mullins, et al., *The Impact of Pipeline Drugs On Drug Spending Growth,* 20 Health Affairs 210, 213 (Sept./Oct. 2001).

modifying information costs and resistance to substitution.[26] Marketing encourages substitution of a new patented drug in place of older generic drugs.[27]

DTC campaigns also build consumer demand, encouraging the patient to ask for a prescription by name. Advertising shifts the demand curve for prescription drugs to the right.[28] In 2000, the most heavily advertised drugs accounted for 47.8% of the $20.8 billion increase in US retail spending on prescription drugs.[29]

Drug companies also spend billions of dollars to employ product representatives, who meet with doctors in various venues. These efforts encourage particular prescribing habits[30] and shift demand between drugs through substitution.[31] In 2000, US promotional spending on prescription drugs totaled $15.7 billion.[32]

Other government agencies also influence pharmaceutical marketing. The Department of Health and Human Services applies Medicare fraud and abuse laws to the practices of drug representatives, forbidding remuneration to encourage particular prescribing practices within federal programs.[33] Fraud and abuse rules may also be implicated in the $7.9 billion of free samples given to doctors in 2000 and the $1.9 billion of educational conferences given to doctors.[34] Federal law prohibits the sale of a drug sample, hindering arbitrage of this product by physicians.[35] The Prescription Drug Marketing Act of 1987 forbids the domestic resale of deeply-discounted drugs sold to certain hospitals.[36] This Act permits drug companies to offer low prices to VA and certain non-profit institutions, without fear of domestic arbitrage.

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[26] Philips, *supra* note 8, at ch. 12. The seminal paper on price dispersion and information costs is G. J. Stigler, *The Economics of Information*, 69 J. of Political Economy 213-14 (1961).

[27] Canadian Institute for Health Information, *supra* note 24, at 37.

[28] NIHCM Foundation, *supra* note 24, at 2 (DTC advertising increases consumer sales of patented pharmaceuticals); Congressional Budget Office, How Increased Competition from Generic Drugs Has Affected Prices and Returns in the Pharmaceutical Industry 20 (July 1998) [hereinafter CBO, Increased Competition].

[29] NIHCM Foundation, *supra* note 24, at 2.

[30] In 2000, the industry employed 83,000 drug representatives at a cost of $4 billion. NIHCM Foundation, *supra* note 24, at 5.

[31] NIHCM Foundation, *supra* note 24, at 7.

[32] NIHCM Foundation, *supra* note 24, at fig. 3. Approximately one third related to one-on-one meetings with doctors, visits to hospitals, or conferences, and only a portion of that could be considered educational. The largest marketing expense is for free drug samples ($7.9 billion in 2000). Id. at 5. In 2000, US unit sales of the 50 most heavily advertised drugs rose at six times the rate of other drugs. Id. at 7 (by number of prescriptions).

[33] Andy Schneider, Taxpayers Against Fraud Education Fund, Reducing Medicare and Medicaid Fraud by Drug Manufacturers: The Role of the False Claims Act 26-36 (Nov. 2003) (review of False Claim Act litigation against drug companies, particularly involving marketing related fraud); Department of Health and Human Services, Compliance Program Guidance for Pharmaceutical Manufacturers, 68 Fed. Reg. 23731, 23733-39 (May 5, 2003).

[34] NIHCM Foundation, *supra* note 24, at 5 (spending figures); Schneider, *supra* note 33, at 26-36 (fraud cases); Department of Health and Human Services, Compliance Program Guidance for Pharmaceutical Manufacturers, 68 Fed. Reg. 23731, 23735-38 (May 5, 2003).

[35] 21 U.S.C. §§ 331(t), 353(d).

[36] Prescription Drug Marketing Act of 1987, 21 U.S.C. § 353(c)(3) (2004).

International arbitrage is also proscribed. Under the Food and Drug Act, foreign produced drugs cannot be imported unless approved by the FDA,[37] creating a non-tariff barrier to international trade. Some drugs are produced in the US and exported to countries with price controls such as Canada.[38] Since the drugs are produced in the US, they arguably comply with FDA rules, and could be re-imported back into the US by arbitrageurs. The US Prescription Drug Marketing Act of 1987 prohibits the re-importation of a prescription drug by anyone other than the manufacturer.[39] The law was intended to address safety concerns for the US pharmaceutical supply chain,[40] but its effect is to prevent international pharmaceutical arbitrage (parallel trade).

Finally, most private purchasers of pharmaceuticals have substitution agendas of their own which are subject to government regulation. Many health plans now require prescriptions to be filled with generic equivalents whenever medically appropriate. US state and federal laws generally support these efforts,[41] while pharmacy laws abroad may restrict generic substitution.[42] Laws supporting substitution by the pharmacist or pharmacy benefit manager erode differential pricing.

b. Intellectual Property (IP) Laws

IP laws support differential pricing by creating legally enforceable rights such as patents and trademarks. Pharmaceutical patents prevent substitution during the patent period by identical compounds. Trademarks support brand identification and differentiation of products to consumers, preventing consumer confusion or unintended substitution.[43] The government may also seize counterfeit drugs. All of these efforts support differential pricing.

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[37] 21 U.S.C. §§ 360(i), 381(a) (2004).

[38] For the company view on price controls, *see, e.g.,* Schneider, *supra* note 33, at 47 ("Pharmaceutical manufacturers have long maintained that government price controls will thwart the development of vital new drugs with the potential to cure diseases and relieve human suffering. The desired alternative, they argue, is a vigorous free market, with prices set through negotiations between buyers and sellers. For this market to work effectively, manufacturers contend, they must retain the right to keep their prices confidential from competitors"). Price controls are discussed in Section IV.C.6 *infra.*

[39] Prescription Drug Marketing Act of 1987, 21 U.S.C. §§ 331(t), 381(d) (2004).

[40] H.R. Rep. No. 100-76, at 7 (1987).

[41] *See, e.g.,* W. Va. Stat. § § 30-5-12 (2004) (allowing pharmacists to substitute generic medicines for brand name medicines without approval from the prescriber) and W. Va. Stat. §23-4-3 (2004) (requiring generic substitution within the Workers' Compensation program).

[42] Patricia Danzon and Johathan D. Ketcham, Reference Pricing of Pharmaceuticals for Medicare: Evidence from Germany, the Netherlands and New Zealand 7 (Nat'l Bureau of Econ. Research Working Paper No. W10007, Oct. 2003) (Germany restricts generic substitution).

[43] Timothy H. Hiebert, Parallel Importation in U.S. Trademark law 151-57 (1994) (discussing the consumer confusion theory underlying the exclusion of parallel imports under trademark law); Warwick A. Rothnie, Parallel Imports 101-05 (1993) (discussing the role of distinct domestic goodwill to successfully exclude parallel goods under trademark law).

In many nations, the first sale of a patented product exhausts the public law rights of the patent holder for that item.[44] The exhaustion rule is a necessary condition[45] to legal domestic arbitrage, as it permits domestic resale by the purchaser without the permission of the patent holder.[46] Exhaustion may be applied on a domestic or an international basis. The domestic exhaustion rule renders parallel imports illegal while the international exhaustion rule removes patent law barriers to international parallel trade.[47] US law only recently rejected the international patent exhaustion rule, and the extent of the rejection may not yet be clear.[48]

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[44] Rothnie, *supra* note 43, at 125-42 (Anglo-Commonwealth patent law), 143-150 (US patent law).

[45] Necessary but not sufficient. Significant price differentials, low transaction costs, and the legal ability to arbitrage are also required. The power of other factors is demonstrated by the persistence of pharmaceutical pricing differentials within the EU, despite a strong internal exhaustion rule and EU firms specializing in pharmaceutical arbitrage. Rothnie, *supra* note 43, at 477, 494-97; *see generally* DG Trade, *supra* note 7, at § 3.

[46] Domestic parallel trade in pharmaceuticals is legal within the EU and the US. *See, e.g.,*Case 187/80, Merck v. Stephar and Exler, 1981 E.C.R. 2063, [1981] 3 C.M.L.R. 463 (parallel drug trade is legal in the EU); Donald S. Chisum, Chisum on Patents §16.03[2] (2003) (the US domestic exhaustion rule); *but see* Case T-41/96, Bayer A.G. v. E.C. Commission, [2001] 4 C.M.L.R. 4 (unilateral acts by pharmaceutical company to choke off supply of drugs to parallel exporters is not actionable under EU law). For book-length treatments of parallel trade, *see* Hiebert, *supra* note (US trademark law); and Rothnie, *supra* note 43 (Anglo-Commonwealth, US and EU patent, trademark and copyright law).

[47] DG Trade, *supra* note 7, at §3.1 ("A country providing for international exhaustion effectively makes parallel imports legal, while a country (or regional group) that provides for national (or regional) exhaustion enables rightholders to act against such imports"). TRIPS does not commit to a position on exhaustion, specifically reserving the issue to domestic law. TRIPS, *supra* note 2, art. 6; Correa, *Implications of Doha, supra* note 3, at 17-18 (citing subparagraph 5(d) of the Doha Declaration). Some commentators writing on the economics of essential medicines mention without critique that US patent law rejects the international exhaustion rule. *See, e.g.,* Jean O. Lanjouw, Intellectual Property and the Availability of Pharmaceuticals in Poor Countries 19-20, n.29 (Center for Global Development, Working Paper No. 5, April 2002) *reprinted in* Innovation Policy and the Economy [hereinafter Lanjouw, Intellectual Property]; and John H. Barton, Differentiated Pricing of Patented Products (WHO, Commission on Macroeconomics and Health Working Paper No. 2, 2001). *See* note 48 *infra* and text accompanying for a critique of the current US patent exhaustion rule.

[48] One distinguished commentator states, without discussion, that the 1994 amendments reject international exhaustion for US patents. Chisum, *supra* note 46, at § 16.05[3]. The amendment was included as part of the Uruguay Round Agreements Act by which the US joined the WTO. Uruguay Round Agreements Act, Pub. L. No. 103-465, 108 Stat. 4809 (1994) (§ 533 of the Uruguay Round Agreements Act amended 35 U.S.C. §271(a) to expand the definition of infringement to include importation into the US of a patented product). The legislative history of this provision is obscure. The House Reports on the Uruguay Round Agreements Act do not include an analysis of Section 533, and the only mention in the summary description is: "amends the definition of infringing activity to include offers for sale and importation of a patented good." H.R. Rep. No. 826(I), at 8. The unofficial summary by the Congressional Research Service merely states: "(Sec. 533) Deems offering to sell or import a patented invention into the United States to be patent infringement." Congressional Research Service, Bill Summary & Status, H.R. 5110 (Pub. L. No. 103-465), 103rd Cong., 2nd Sess. (summary dated Sept., 27, 1994). Four points are important. First, prior to the amendments, US patent law was leaning in favor of the international exhaustion rule. Rothnie, *supra* note 43, at 183; Chisum, *supra* note 46, at §1605[3]; Second, it is not clear at all that Congress intended to overturn the international exhaustion exception by the enactment of § 533. One may declare importation an act of infringement, and yet retain the narrower exception for authorized sales abroad being imported legally under international exhaustion. *But see* Chisum, *supra* note 46, at §16.05[3]. Third, the provision, enacted as part of the Uruguay Round Agreements, was not required, as WTO Members retain domestic flexibility to choose any exhaustion rule. Correa, *Implications of Doha, supra*

Even if one assumes that the US follows the domestic exhaustion rule for pharmaceutical patents, drugs sold in the US, exported to Canada, and then re-imported back into the US arguably qualify for domestic exhaustion.[49] The Prescription Drug Marketing Act of 1987 blocks re-importation by anyone other than the manufacturer, preventing arbitrage.

III. The Legal and Economic Framework for Innovative Drugs

A. The Innovation Theory of IP Law[50]

From ancient times, law and social conventions have supported the right to exclude, enforcing rights to what we call personal property.[51] Persons investing in producing goods are able to reap a reward for their effort because the law creates a property right in the good produced. This property right is exclusive, meaning that other persons cannot take the property without consent or due process.[52] In the language of economics, goods are 'appropriable.' The right to exclude makes personal property more valuable.

At common law, knowledge was not considered personal property,[53] perhaps because the use of information is subject to (at least) two peculiar characteristics. First, it is generally more difficult to exclude other persons from using information, the condition of *inappropriability* [nonexcludibility].[54] Second, while physical goods like corn or wheat are exhausted when used, knowledge may be used without exhaustion, the condition of

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note 3, at 17-18 (citing subparagraph 5(d) of the Doha Declaration). Finally, the heuristic of optimality (discussed in Section IV *infra*) suggests that any provision which strengthens drug patent rights will enhance beneficial innovation only if patent rents were sub-optimal. This issue was not demonstrated to Congress in the legislative history to the 1994 amendment. For a discussion of Anglo-Commonwealth views on international patent exhaustion, *see* Rothnie, *supra* note 43, at 183-85.

[49] *See* Rebecca S. Eisenberg, *The Shifting Functional Balance of Patents and Drug Regulation,* 19 Health Affairs 119, 129-32 (Sept./Oct. 2001) [hereinafter Eisenberg, *Patents and Drug Regulation*]. Re-imported patented drugs are produced in the US under proper authority, legally exported to a second country (such as Canada) and then re-imported by a third party, arguably exhausting US patent rights over the pills themselves. There is no evidence that the 1994 modifications to 35 U.S.C. § 271(a) were intended to waive the domestic exhaustion rule on re-imported goods. *See* note [48], *infra*.

[50] An independent ground for patent law is the contract or disclosure theory, which posits that patents are socially preferable over trade secrets due to the socially useful disclosure function. Vincenzo Denicolo & Luigi Alberto Franzoni, *The Contract Theory of Patents*, 23 Int'l Rev. of L. & Econ. 365, 366-68 (2004). In pharmaceuticals, the national drug regulatory agency process requires disclosure in any case, which makes the contract theory less applicable.

[51] *See, e.g., Exodus* 20:15 (NRSV) ("You shall not steal"). The right to exclude from land developed much later, and is not yet fully ascendant in some traditional communities.

[52] With the abolition of slavery, the same can now be said of the provision of personal services.

[53] Wheaton v. Peters, 33 U.S. (8 Pet.) 591, 657 (1834). The first English copyright statute was the Statute of Anne, 8 Ann., c. 19 (1710) and the first English "patent" statute was the Statute of Monopolies, 21 Jac. 1, c. 3 (1624).

[54] Empirical research challenges the conclusion that inappropriability requires patent protection. In a survey of US manufacturing firm responses to inappropriability, patents were found to be less important than secrecy, lead time advantages, and the use of complementary marketing and manufacturing capabilities. Wesley M. Cohen, Richard R. Nelson & John P. Walsh, Protecting Their Intellectual Assets: Appropriability Conditions and Why U.S. Manufacturing Firms Patent 2, 24-25 (Nat'l Bureau of Econ. Research Working Paper No. W7552, Feb. 2000).

inexhaustibility[nonrival].[55] The twin conditions of inappropriability and inexhaustibility permit the widest possible dissemination of knowledge without creating shortages.[56]

Unfortunately, if *homo econimus* understands that the fruits of research will be inappropriable, then the market offers no financial incentive to innovate.[57] Others will gladly use it without compensating the innovator. The innovator cannot capture the positive externality, undermining the incentive to innovate.

Pharmaceutical research companies strongly embrace this 'innovation' thesis. Pharmaceutical research companies spend many millions of dollars over a number of years to bring a newly patented product to market. As the industry saying goes, "How much does it cost to make a new drug? The first pill costs $800 million; after that, each pill costs 20 cents each." The industry is characterized by high fixed costs and low variable costs. The first mover (a pharmaceutical research company)[58] incurs all research costs (including failed programs), while free riders (subsequent movers such as generic drug companies) may have limited barriers to entry and a significantly lower cost structure.[59]

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[55] While knowledge is not destroyed through use, it may lose value. Market-moving financial information loses its value quickly, particularly as market participants act on the information. From a societal perspective, however, knowledge does not lose value through use, but adds to the public domain.

[56] This point is occasionally overlooked in this context. In his critique of the essential medicine agenda in TRIPS, Alan Sykes missed the nonrival nature of pharmaceutical patents by analogizing compulsory licensure to physical expropriation. Alan O. Sykes, *TRIPs, Pharmaceuticals, Developing Countries, and the Doha "Solution,"* 3 Ch. J. Int'l L. 47, 56 (2002). William Landes and Richard Posner argue that some forms of IP are rival, particularly trademarks and personal likenesses. William M. Landes & Richard A. Posner, *Indefinitely Renewable Copyright*, 70 U. Chi. L. Rev. 471, 484-86 (2003). Trademarks and personal likenesses indicate origin rather than being knowledge *per se*. Other forms of IP are nonrival in the classic sense, although nonrival use will certainly undercut monopoly pricing and affect *ex ante* innovation incentives.

[57] The economic model overstates the case. Knowledge expanded in the centuries prior to the adoption of patent law. Important books were written before the Statute of Anne. Partial explanations include research for non-economic motives, such as curiosity. The model also overreaches to say that knowledge is fully inappropriable. In both historic and contemporary times, transmission of knowledge has never been immediate and barrier free, as any student or professor can attest.

[58] Pharmaceutical companies have traditionally been categorized as either research companies (Pfizer, Merck) or generic companies without significant research programs (Cipla, Mylan). The United States trade association of research pharmaceutical companies is the Pharmaceutical Research and Manufacturers of America (PhRMA), www.phrma.org. The international trade association of pharmaceutical research company associations is the International Federation of Pharmaceutical Manufacturers Associations (IFPMA), www.ifpma.org. Generic drug companies have their own trade associations. In recent years, these distinctions have blurred as research companies have invested in generic subsidiaries and as generic companies have begun substantial research programs. It may be more accurate to describe research or generic lines of business, rather than companies *per se*.

[59] These assumptions are openly challenged in many industries. For most industries, it appears that patents play a relatively modest role in making invention non-appropriable by free riders. Wesley M. Cohen et al., Protecting Their Intellectual Assets: Appropriability Conditions and Why U.S. Manufacturing Firms Patent (or Not), 6 (Nat'l Bureau of Econ. Research, Working Paper No. 7552, 2000); Richard C. Levin, A New Look at the Patent System, 76 Amer. Econ. Rev. 199, 200-01 (1986); Richard C. Levin et al., Appropriating the Returns from Industrial Research and Development, in 3 Brookings Papers on Economic Activity 783 (Martin Neil Baily & Clifford Winston eds., 1987); Edwin J. Mansfield, Patents and

Intellectual property law offers an allegedly second-best solution to this impasse,[60] "promot[ing] 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."[61] Patents are the Constitution's favorite monopoly.[62] For patents, the period of exclusivity is not less than 20 years after filing, under federal law and the TRIPS Agreement.[63]

IP law enhances the appropriability of certain types of information, for a limited time, as an incentive to innovate.[64] Absent exclusivity, drug companies will be less likely to recover research costs on innovative products and will have greatly diminished incentives to invest in new research.[65] Innovator companies also command many other non-patent tools to enhance appropriation, particularly incumbent companies with strong market

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Innovation: An Empirical Study, 32 Mgmt. Sci. 173 (1986). For a discussion of the conditions of appropriability in pharmaceuticals, *see infra* [n. 64].

[60] William D. Nordhaus, Invention, Growth, and Welfare: A Theoretical Treatment of Technological Change 38 (1969) ("It should be noted here that there is nothing inevitable about the inappropriability of invention. Legislation involving patents and trade secrets considerably enlarges the ability of firms to appropriate their inventive output; in other words, patent laws internalize the externality"). Many other scholars have made this point. *See, e.g.,* Tomas J. Philipson & Stéphane Mechoulan, Intellectual Property & External Consumption Effects: Generalizations from Pharmaceutical Markets 3, 8, 14-15 (Nat'l Bureau of Econ. Research, Working Paper No. 9598, April 2003) ("In the private case, it is well-understood that efficient competition ex-post leads to insufficient R&D incentives ex-ante, which is of course the common second-best rationale for patents") (at 3).

[61] U.S. Const. art. I., § 8, cl. 8 ("To 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").

[62] A bare patent does not grant market power if the invention is unimportant or easily substitutable. Kenneth W. Dam, *The Economic Underpinnings of Patent Law*, 23 J. Legal Studies 247-51 (1994). Pharmaceutical patents of blockbuster drugs are a strong case of patents creating market power, and may be more appropriately denominated as a monopoly. The pharmaceutical industry eschews the monopoly label, but nevertheless defends the patent system as essential to encourage R&D. One cannot have it both ways.

[63] TRIPS, *supra* note 2, at art. 33. TRIPS permitted many developing countries to implement on a delayed basis. TRIPS, *supra* note 2, at arts. 65 & 66. After extensions, most developing countries must implement the TRIPS Agreement by January 1, 2005, but the 30 'least developed countries' may defer full implementation for pharmaceutical products until 2016. Doha Declaration, *supra* note 5, at ¶ 7. TRIPS merely sets minimum periods of patent protection; the US could still unilaterally extend patent protection, and has done so with copyright. Unilateral extensions by the US would increase the problems of arbitrage identified in this article.

[64] This incentive is the intent of patent law, but empirical work in economics challenges the notion that patents are vital to support innovation in most industries. Ashish Arora, Marco Ceccagnoli & Wesley M. Cohen, R&D and the Patent Premium 4, 34-35 (Nat'l Bureau of Econ. Research Working Paper No. 9431, Jan. 2003) ("Empirical work also suggests that the inducement provided by patents for innovation is small"); Cohen, *supra* note 54, at 2, 24-25 (40 years of empirical data demonstrates that patents don't improve innovation, with exceptions in pharmaceuticals; study concludes that patents are not the most significant mechanisms for appropriating returns to innovation in most industries, with secrecy, lead time and complimentary capabilities leading). In pharmaceuticals, secrecy is not an option with the public drug application process. In pharmaceuticals, the evidence is stronger of a linkage between patents and innovation. Arora, et al., *supra*, at 4-5, 35. Arora's study found a significant patent premium (ie., a positive return on investment), particularly in biotechnology, medical instruments and drugs. Id. at 30, 34-35.

[65] Arora's study was apparently the first to test this proposition empirically, finding that US R&D would fall by 35% in the absence of patent protection. Arora, et al., *supra* note 63, at 31-34.

positions.[66] On the other hand, the cumulative effect of patent law and non-patent support for appropriation allows the innovator to charge a higher price under monopolistic conditions, and delays entry of knowledge into the public domain.

The tension between the development and dissemination of knowledge permeates the most compelling issues in pharmaceutical IP policy. Patent doctrines such as scope,[67] experimental use,[68] and fair use[69] may also be adjusted to balance innovation and dissemination.[70] Too many restrictions on inappropriability (i.e., excessive IP rights), needlessly raises cost and restricts access to important pharmaceuticals.[71] Too few might throttle the R&D enterprise, and society will forgo valuable qualitative improvements. It is far from clear that current policy strikes an appropriate balance. James Boyle expresses his doubts in the nearby field of copyright law:

> The economic definition of chutzpah is the industry that demands a legalized monopoly, and then, once given it even though the evidence was weak, insists on the state's aid in price discrimination, the better to wring every last cent of consumer surplus out of their customers.[72]

B. The FDA and the Hatch-Waxman Act[73]

Marketing a pharmaceutical does not require a patent. In most nations, the DRA controls access to the domestic market. In the US, the FDA regulates the safety and efficacy of pharmaceuticals.[74]

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[66] *See* Jonathan M. Barnett, *Private Protection of Patentable Goods*, 25 Cardozo L. Rev. 1251 (2004).

[67] Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 Colum. L. Rev. 839 (1990) *passim* (examining the potential role of patent breadth in fine tuning the efficiency of the patent system). Many economic studies examine elements of this question. *See, e.g.,* Nordhaus, *supra* note 59, at 70-90; F.M. Scherer, *Nordhaus' Theory of Optimal Patent Life: A Geometric Reinterpretation*, 62 Am. Econ. Rev. 422-27 (1972) [hereinafter Scherer, *Optimal Patent Life*]; William D. Nordhaus, *The Optimum Life of a Patent: Reply*, 62 Am. Econ. Rev. 428 (1972) [hereinafter Nordhaus, *The Optimum Life of a Patent*]. For a recent example, *see* Philipson & Mechoulan, *supra* note 59, at 8-13.

[68] Rebecca Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. Chi. L. Rev. 1017 (1989) [hereinafter Eisenberg, *Patents and the Progress of Science*]; Rebecca Eisenberg, *Proprietary Rights and the Norms of Science in Biotechnology Research*, 97 Yale L.J. 177 (1987). [hereinafter Eisenberg, *Proprietary Rights*].

[69] Maureen A. O'Rourke, *Toward a Doctrine of Fair Use in Patent Law,* 100 Colum. L. Rev. 1177 (2000).

[70] Dam, *supra* note 61, at 261-68.

[71] This point assumes that increased consumption of patented pharmaceuticals creates net positive externalities, i.e. that society would benefit from increased access and consumption of the drug. Philipson & Mechoulan, *supra* note 59, at 9. This assumption will be challenged in the discussion of antibiotic resistance in Section III.D.3 *infra.*

[72] James Boyle, *Cruel, Mean, or Lavish? Economic Analysis, Price Discrimination and Digital Intellectual Property,* 53 Vand. L. Rev. 2007, 2037 (2000).

[73] Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended in scattered sections of 15, 21, 28 and 35 U.S.C.) [hereinafter Hatch-Waxman Act].

[74] The FDA regulates the drug approval process. 21 U.S.C. § 355 (2004). Under the Hatch-Waxman Act, the FDA also influences the patent process, since Hatch-Waxman extends the patent for half of the period that a drug is undergoing clinical trials, plus the full amount of time spent in the FDA approval process. 35 U.S.C. §§ 155, 155A and 156 (2004). In addition, the FDA is authorized to grant non-patent "exclusive

When examining the incentives for pharmaceutical innovation, the important period is not the length of the patent (20 years), but the length of the *exclusive marketing period*.[75] In the late 1990's, the US pharmaceutical exclusive marketing period was approximately fourteen years.[76] The FDA approval process is largely responsible for the six-year difference.

In 1984, Congress modified patent and FDA law in an attempt to strike a better balance between pharmaceutical innovation (quality) and affordable medications (access and cost).[77] The Hatch-Waxman Act brought generic drugs to the market more quickly while strengthening innovation incentives through extended patent terms and exclusive marketing periods.[78] Approval of generic drugs soared following Hatch-Waxman, but the net exclusive marketing period remained relatively unchanged.[79]

The FDA regulatory process may also lengthen the exclusive marketing period. The FDA may grant additional exclusive marketing periods for first-mover generic drugs,[80] certain orphan drugs,[81] and for compliance with social goals such as testing drugs for efficacy and safety on children,[82] independent of the patent system. Pharmaceutical research companies may be abusing these provisions.[83]

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marketing" periods to certain drugs, whether patented or not. 21 U.S.C. §§ 355a(a) (pediatric studies of drugs), 360aa (orphan drugs) (2004).

[75] The term *exclusive marketing period* means the actual period during which a pharmaceutical company sells a FDA-approved drug in the United States without direct competition. The legal sources of this period include patent law, non-patent "exclusive marketing" rights granted by the FDA under Hatch-Waxman, *see* note 72 *supra,* and the use of litigation and agreements to forestall competitive entry, *see* notes 82-83 *infra.*

[76] CBO, Increased Competition, *supra* note 28, at 45-48.

[77] *See, e.g.,* Elizabeth Stotland Weiswasser & Scott D. Danzis, *The Hatch-Waxman Act: History, Structure, and Legacy,*71 Antitrust L. J. 585 (2003). Philipson and Mechoulan describe this balance in the language of economics: "Appropriate policy must *simultaneously* solve the externality problem ex-post and the R&D problem ex-ante"). Philipson & Mechoulan, *supra* note 59, at 12 (emphasis in original).

[78] Traditionally, patent law regulates the economic incentives of innovation while FDA law controls efficacy and safety. Under the Hatch-Waxman Act, FDA provisions stray into the domain of patent laws with non-patent exclusive marketing periods. *See supra* notes 72-73 and text accompanying.

[79] CBO, Increased Competition, *supra* note 28, at viii-ix, 38 (Hatch-Waxman's "decline of roughly three years in the average time before generic entry is almost exactly offset by the average increase in patent terms from Hatch-Waxman extensions.")

[80] 21 U.S.C. § 355(j) (2004).

[81] 21 U.S.C. §§ 360aa-360ee (2004).

[82] 21 U.S.C. § 355a (2004).

[83] For example, the number of putative orphan drugs qualifying for tax credits and extended exclusive marketing periods have soared as companies have narrowly defined markets to remain under the 200,000 person threshold. Steven R. Salbu, *AIDS and Drug Policy: In Search of a Policy*, 71 Wash. Univ. L. Q. 691, 692, 704-06 (1993) (FDA designated AZT as an orphan drug in 1987; more than half of AIDS drugs as of August 31, 1991 were designated orphans); John J. Flynn, *The Orphan Drug Act: An Unconstitutional Exercise of the Patent Power,* 1992 Utah L. Rev. 389, 389-403 (FDA designated early AIDS drugs such as AZT, and other best-selling drugs such as EPO and Taxol as orphan drugs). The tax expenditure on the Orphan Drug Act is $200 million per year, not including the cost of the grant of market exclusivity. Joint Committee on Taxation, Estimates of Federal Tax Expenditures for FYs 2004-2008 (Joint Committee Print, Dec. 22, 2003). Public Citizen notes the inefficiency of the incentive mechanism: pediatric tests cost only $3.9 million per drug on average, but the six-month patent extension can result in

After a patent or exclusive marketing period expires, competition by generic drugs is not automatic. Generic drugs must receive FDA approval as well, albeit under an abbreviated process. The generic entry process can take some time, particularly if existing data on safety and efficacy cannot be used, or if the manufacturing processes are complex. Pharmaceutical research companies have resorted to strategic litigation and collusive agreements to lengthen effective exclusive marketing periods.[84] These abuses prompted amendments to Hatch-Waxman in 2003.[85] Pharmaceutical research companies are already responding with new tactics keep generic drugs off the market by denying the generic companies an adequate financial return for the expensive process of gaining generic approval and gearing up for production.[86]

Amending Hatch-Waxman is unlikely to achieve an optimal balance between R&D quality and financial access to drugs. In this arena, Congress requires many years to reach consensus and the results have generally reified the status quo, without regard for the globally optimal level of pharmaceutical R&D.[87] Hatch-Waxman fails to distinguish between truly innovative drugs addressing urgent global needs and 'me-too'[88] drugs targeting the relatively minor nuisances of Western affluence. Hatch-Waxman also ignores the global nature of pharmaceutical R&D; this stance has resulted in the US paying the highest patented drug prices in the world, as the largest market without significant price controls.

C. Other Constraints on Drug Pricing

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huge financial rewards exceeding $1 billion. Public Citizen, The Other Drug War II: Drug Companies Use and Army of 623 Lobbyists to Keep Profits Up 4 (Public Citizen's Congress Watch, June 12, 2002). The FDA estimates the total cost of the pediatric testing initiative from 2001 to 2021 to be $14 billion, approximately equal to the proposed 5 year AIDS program. U.S. Food and Drug Administration, The Pediatric Exclusivity Provision: Status Report to Congress (Jan. 2001).

[84] Federal Trade Commission, Generic Drug Entry Prior to Patent Expiration: An FTC Study 13-23 (July 2002).

[85] Prescription Drug and Medicare Improvement Act of 2003, 21 U.S.C. § 355(j) and tit. IX (uncodified, Pub. L. No. 108-173), 117 Stat. 2448 (2004). The Congressional Research Service prepared a summary of the Act on June 13, 2003 which provides some guidance on Congress's intent in amending Hatch-Waxman. *See* Congressional Research Service, Prescription Drug and Medicare Improvement Act of 2003 (Bill Summary and Status, S.1, 108th Cong.) (June 13, 2003) *available at* www.thomas.loc.gov. For a recent article describing proposed amendments to Hatch-Waxman, authored prior to the passage of the 2003 Act, *see* Laura J. Robinson, *Analysis of Recent Proposals to Reconfigure Hatch-Waxman,* 11 J. Intell. Prop. L. 47 (2003)

[86] Leila Abboud, *Drug Makers Use New Tactic to Ding Generics*, Wall St. J., Jan. 27, 2004, at B1.

[87] CBO, Increased Competition, *supra* note 28, at 48.

[88] In recent years, Health Canada has designated only 7% of drugs approved in Canada as Category 2 breakthrough drugs. Maria Barrados, et al., 1998 Report of the Auditor General of Canada, ch. 17, ¶17.93 (Sept. 1999) *available at* http://www.oag-bvg.gc.ca. In a review of the British experience, Hancher is critical of the prevalence of me-too drugs which do not offer significant therapeutic advances. Leigh Hancher, Regulating for Competition 51 (1990). Some 'me-too' drugs are offer significant clinical advances when used in combination with other drugs, particularly in avoiding the development of resistance. Monotherapy for AIDS ran a significantly greater risk of developing resistance than the current practice of triple-combination therapy. [population health issue; but FDC drugs are really different classes]

Pharmaceutical research companies do not enjoy unconstrained monopoly power to set prices on patented drugs. In each major national market, regulatory systems and buyer monopsony power may create countervailing pricing power. In some countries, the government sets pharmaceutical prices by regulatory process, including reference pricing[89] and rate setting.[90] In others, price regulation occurs when the government enters the market as a purchaser and acts with monopsony power.[91] Private payors (health plans or their agents such as pharmacy benefit managers) may either free ride on the government prices, or utilize their own market power to negotiate prices. In the US, the uninsured or others without market power often pay the highest prices.[92]

The net result is differential pricing, charging different net prices to various customers for the same product. Pharmaceutical research companies segment markets along efficient boundaries, generally political borders or payor classes. Pharmaceutical differential pricing exists among different countries (such as Canada, US, and South Africa) and among different buyers or payor classes within countries such as the US (Medicare, Medicaid, Veterans Affairs, federal employees, private health plans, and individuals).

D. Pharmaceutical Market Failures[93]

1. Drugs for Neglected Diseases[94]

Orphan drugs treat conditions suffered by a relatively small number of patients, frequently too few to provide a revenue stream sufficient to recover R&D costs.[95]

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[89] Danzon & Ketcham, *supra* note 42 (reference price systems in Germany, The Netherlands, and New Zealand).

[90] House of Commons, Examination of Witnesses (Jan. 23, 2002) (examination of Dr. John Patterson) ("Prices almost never go up on medicines in this country [England], as you saw from the report to Parliament in December. In brief, the PPRS is a scheme which caps profits and profitability in our industry at a level equivalent to the average return on capital of the FT 100.") The US effectively sets rates for government purchase of services from physicians and hospitals, but generally not for pharmaceuticals.

[91] In the US, the recently-enacted Medicare Act disabled federal monopsony power in the purchase of outpatient prescription drugs under Medicare. Medicare Prescription Drug Improvement and Modernization Act of 2003, Pub. L. No. 108-173, § 301, 42 U.S.C. §1395 et seq. [§ 1808(c)(1)(C) of the SSA] (2004). [search act herein]

[92] CBO, Increased Competition, *supra* note 28, at xi.

[93] The following discussion is certainly not an exhaustive list of pharmaceutical market failures, but focuses on major innovation issues.

[94] The phrase *tropical diseases* may be misleading since some neglected conditions are not caused by tropical microbes or parasites. Other alternative terms in the literature include *neglected diseases, developing world diseases, Southern diseases,* and *diseases of the poor*. In this article, the terms *neglected diseases* and *tropical diseases* will be used. Jean Lanjouw has compiled a list of the 20 most important tropical diseases, with at least 99% of their disease burden in low-income countries. Jean O. Lanjouw, A Patent Policy Proposal for Global Diseases tab. 1 (June 11, 2001) (on file with author) [hereinafter, Lanjouw, Global Diseases]. *See also* Keith E. Maskus, *Ensuring Access to Essential Medicines: Some Economic Considerations,* 20 Wisc. Int'l L. J. 563, 568-70 (2002) [hereinafter Maskus, *Essential Medicines*] (public incentives are needed to stimulate demand for tropical diseases); and Philipson & Mechoulan, *supra* note 59, at 21. Henry Grabowski appears to have been the first to designate tropical diseases as a category of 'orphan diseases.' Henry Grabowski, *Patents, Innovation and Access to New Pharmaceuticals*, 5 J. of Int'l Econ. L. 849 (2002).

Pharmaceutical companies are said to be unlikely to undertake R&D for potential annual markets under $250 million (presumably for the 14 years of effective exclusive marketing).[96] The US addresses this market failure domestically through tax credits for domestic orphan drug research[97] and longer exclusive marketing periods under Hatch-Waxman.[98]

Neglected disease drugs are quite different: the patients are not few in number, but merely impoverished and primarily located in low-income countries. Lacking an OECD market[99] for these drugs or vaccines, pharmaceutical research companies do not invest the necessary R&D, despite pressing global health needs.[100] The global R&D output of new drugs to treat tropical diseases over the past quarter century has been exceedingly modest, less than 1%.[101] The profit motive does not fully explain this dearth, since the majority of global health research funding is provided by governments or private non-profit foundations,[102] who are not constrained by the pricing signals of the marketplace and could conceivably respond to priority global health needs instead. Many global public health groups are attempting to re-orient public and non-profit spending to address the misallocation of R&D away from the needs of developing countries, such as the "10/90 Gap" project by the Global Forum for Health Research.

For the private sector, a market-based approach is required. Several researchers have proposed solutions to the problem of neglected disease drugs. IP rights and the TRIPS Agreement figure prominently in these debates.

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[95] A drug may be designated as an orphan under US tax law for conditions which exceed the 200,000 numerical limit, so long as "there is no reasonable expectation that the cost [R&D]…will be recovered from sales in the United States of such drug." 26 U.S.C. § 45C(d)(1)(B); *see also* 21 U.S.C. § 360bb(2).

[96] Michael Kremer, *Creating Markets for New Vaccines: Part I: Rationale & Part II: Design Issues*, in Innovation Policy and the Economy (Adam B. Jaffe, et al, eds., 2001) 35, 73, 76; Jason C. Hsu & Eduardo S. Schwartz, A Model of R&D Valuation and the Design of Research Incentives 29 (Nat'l Bureau of Econ. Research Working Paper No. 10041, Oct. 2003).

[97] Orphan Drug Act of 1983, Pub. L. 97-414, 96 Stat. 2049 (codified in 21 U.S.C. §§ 360aa-360ee and scattered sections of 26 U.S.C.) [hereinafter *Orphan Drug Act*].

[98] *See supra* notes 72-73 and text accompanying.

[99] Herein, *OECD market* means the residents of the richer, developed countries of the world, largely in the Northern hemisphere. Residence in an OECD member country is a reasonable proxy for this group. In low- and medium-income nations, wealthy elites and Western expatriates should also be included in the term OECD market.

[100] Pecoul, et al., *Access to Essential Drugs in Poor Countries: A Lost Battle?*, 281 J. Am. Med. Ass'n 361, 364 (1999) ("It appears that pharmaceutical R&D is abandoning tropical diseases"). Profit maximizing companies minimize R&D for conditions common in the developing (charity) world and focus on conditions endemic largely in the developed (commercial) world. More drugs for conditions such as ADHD and lifestyle drugs such as Viagra and fewer discoveries for neglected diseases with much more significant global disease burdens. For a working list of global diseases, *see* Lanjouw, Global Diseases, *supra* note 92, at tab. 1.

[101] Pecoul, et al., *supra* note 98, at 364-65 (1975-1997 data). Of the few introductions, two were derived from veterinary R&D. *Id.* at 365 (Table 2).

[102] With 1998 data, global health R&D funding from private for-profit sources was estimated at $30.5 billion or approximately 42% of the global total. Global Forum for Health Research, Monitoring Financial Flows for Health Research 2001 at 7 (GFHR/WHO 2001).

a. The Role of IP Laws in Making a Market for Neglected Diseases

Jean Lanjouw and Alan Sykes support the enactment of IP laws in low-income countries to encourage the development of local markets for treating neglected diseases.[103] Lanjouw cites empirical results from India suggesting that implementation of TRIPS is encouraging the largest Indian pharmaceutical companies to invest in R&D for new chemical entities (NCEs),[104] but those NCEs are either me-too generics or target global diseases.[105] Sykes himself critiques Scherer on the question of the net value of IP laws for developing countries, placing his trust on the huge disease burden in the developing world, which should stimulate markets if patents were available. Sykes thus looks to use IP laws to extract a greater portion of consumer surplus from the developing poor, in order to strengthen the incentives to innovate.[106]

Strong IP laws in low-income countries are not sufficient to create new markets for neglected disease drugs. If most patients in such countries are unable to purchase neglected disease drugs in commercial quantities and prices, the offer of patent protection will not stimulate R&D.[107] An exclusive offer to sell drugs at a loss is not valuable.[108]

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[103] Lanjouw, Global Diseases, *supra* note 92, at 4; Sykes, *supra* note [ ] at 58-62.

[104] Jean O. Lanjouw, The Introduction of Pharmaceutical Product Patents in India: 'Heartless Exploitation of the Poor and Suffering?' (Nat'l Bureau of Econ. Research Working Paper No. 6366, Jan. 1998).

[105] Hannah E. Kettler & Rajiv Modi, *Building Local Research and Development Capacity for the Prevention and Cure of Neglected Diseases: The Case of India*, 79 Bull. World Health Org. 742, 744-45 (2001) (Indian companies are likely to target the largest markets, ie. for global diseases rather than neglected diseases). A decade after the signing of TRIPS, a leading Indian pharmaceutical company reports that indeed its R&D budgets are growing rapidly, from 2.7% of sales in 2000 to 7.6% in 2003 and a projected 10% in 2004, but the primary output are ANDAs, that is, generic pharmaceuticals. Adam Levitt, Dr. Reddy's Laboratories: Driving Growth 17-25 (Bear Stearns Healthcare Conference, Sept. 8, 2003) (on file with author) [hereinafter Levitt, Dr. Reddy's Laboratories]. The primary NDA filed by the company is amlodipine maleate, which is the salt version of an innovative drug, Norvasc. The NDA is being opposed in federal court by the innovator company. Id. at 20. Of the eight NCEs in the company's pipeline, seven will treat global diseases such as diabetes, cancer, metabolic disorders and cardiovascular disease. The eighth is an anti-infective drug, also for global diseases, but with more applicability in developing countries. Id. at 27. These are hardly the type of innovations that Lanjouw hoped for, and in fact this activity could hurt global innovation by reducing expected patent rents to innovator companies through early generic entry by aggressive Indian companies.

[106] Sykes, *supra* note [ ], at 61-62.

[107] The relative size of the commercial and non-commercial markets is important here. The growth of India's middle and upper classes is or will be sufficient one day to support commercial pricing of innovative drugs for conditions endemic only to the developing world. PhRMA companies do recognize a growing middle class market in these nations. Merck & Co, Inc., Form 10-k (filed with the SEC on Mar. 10, 2004) at 14 ("In recent years, the Company has been expanding its operations in countries located in Latin America, the Middle East, Africa, Eastern Europe and Asia Pacific where changes in government policies and economic conditions are making it possible for the Company to earn fair returns. Business in these developing areas, while sometimes less stable, offers important opportunities for growth over time."). At that point, the condition becomes a *global disease* in my lexicon, as analyzed in Section III.D.2 *infra.* For a discussion of the internal arbitrage dangers in these situations, *see infra* Section V.E.

[108] Maskus, *Essential Medicines, supra* note 92, at 574 (casting doubt on the efficacy of patents to improve R&D on neglected drugs); Kettler & Modi, *supra* note 102, at 742 (Indian pharmaceutical companies will still require financial incentives to research and develop drugs for neglected diseases). A recent study of neglected vaccine projects found patent incentives to be completely ineffective. Hsu and Schwartz, *supra* note 94, at 37, 43-45.

Profit-maximizing Indian drug companies will focus on their best economic opportunities;[109] neglected disease drugs are not be at the top of that list.[110] In fact, several leading Indian drug companies derive most of their profits from sales in the US, including several high-profile generic drug applications.[111] The absence of pharmaceutical patents in India was the proximate cause of India's vibrant generic pharmaceutical sector. Implementation of TRIPS will hinder this path of development for other countries.

Nevertheless, Lanjouw and Syke's focus on creating and encouraging markets is helpful, and requires a qualification of my previous definition of neglected disease drugs: a market of $250 million per year is necessary to incentivize R&D *at current OECD cost structures.* Non-OECD pharmaceutical research companies may have significantly lower cost structures, enabling R&D on disease markets below the $250 million threshold. Cipla, Ltd. and other Indian pharmaceutical companies pay their India-based chemists and investigators a fraction of the prevailing OECD pharmaceutical company research wages. These companies may also be better poised to understand and respond to the developing market and less likely to discount the actual market size due to unfamiliarity. Network effects and sunk costs are also present in pharmaceutical sales and marketing: while OECD companies have invested in marketing systems in OECD countries, emerging companies invest in regional markets heretofore overlooked by OECD companies,[112] and invest in process developments to lower production costs.[113]

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[109] Kettler & Modi, *supra* note 102, at 745. For the leading Indian pharmaceutical company, in early 2004 only a negligible percentage of sales were of New Chemical Entities (NCEs). Most sales were either active pharmaceutical ingredients (APIs, i.e. intermediate ingredients for drugs) to the US and Europe or branded (generic) formulations sold in India and other less regulated markets. Levitt, Dr. Reddy's Laboratories, *supra* note 102, at 9-10. *See also supra* note 102.

[110] Jean O. Lanjouw and Iain Cockburn, *New Pills for Poor People?: Empirical Evidence After GATT*, 29 World Development 265-89 (2001) (their survey of Indian drug firms in 1998 found only 16% of their R&D targeted developing country markets). In fiscal year 2002-2003, Cipla's major innovative introduction was TIOVA, a long-acting bronchodilator for Chronic Obstructive Pulmonary Disease (COPD), a global disease. Cipla also launched a new generic ARV fixed dose combination. Cipla Sixty-Seventh Annual Report 2002-2003 5 (available from the company and on file with author) [hereinafter Cipla 2002-2003 Annual Report].

[111] *See, e.g.,* Rasul Bailay, *Cipla May Find Right Rx for Success: Indian Drug Firm Partners With Peers in U.S. to Crack No. 1 Market for Generics*, Wall St. J., Oct. 20, 2003, at A15; Cipla 2002-2003 Annual Report, *supra* note 106, at 7 ("During the year, Cipla's strategic alliances with leading generic companies in the USA and Europe were expanded to include additional products and projects. Currently, there are nearly 50 such projects in various stages of development in the USA alone."). For Dr. Reddy's Laboratories, the US market accounted for 57% of 2003 gross margin. Levitt, Dr. Reddy's Laboratories, *supra* note 102, at 11.

[112] India, Russia, China, Brazil, Mexico, Africa and other "less regulated" markets such as Mexico and Brazil are major markets for Indian companies such as Dr. Reddy's Laboratories. Levitt, Dr. Reddy's Laboratories, *supra* note 102, *passim*. *See also* Kettler & Modi, *supra* note 102, at 743 (describing the Indian pharmaceutical industry).

[113] Kettler & Modi, *supra* note 102, at 743-45 (but Kettler and Modi do not assume an Indian comparative advantage in cost). Nor are lower cost structures limited to non-OECD companies. Japanese pharmaceutical research companies have recently proven very successful in drug innovation through relatively low-cost research methods. Peter Landers, *Back to Basics: With Dry Pipelines, Big Drug Makers Stock up in Japan; Shunning High-Tech Gizmos, the Asian Scientists Score with Traditional Lab Work*, Wall St. J., Nov. 24, 2003, at A1.

Most neglected disease conditions lack a market not because of the absence of IP rights in low-income nations, but because of the poverty of the patients. Perhaps the best description of a neglected disease drug is that market innovation is unlikely because the target population will require the drug or vaccine to be distributed for free or below the lowest possible amortized cost. Any such drug will require non-market funding for innovation, even in the strictest IP regime.

b. Neglected Disease Innovation in the Absence of a Commercial Market: Donor Purchase Commitments

In the absence of truly commercial markets for neglected disease drugs, some other mechanism must be found to support innovation. Michael Kremer's model of a donor purchase commitment is a prominent example.[114] If the market threshold for R&D is truly a market of $250 million per year for 14 years, a donor such as the Global Fund could make binding purchase commitments for a safe and effective neglected disease drug or vaccine. Several conditions must apply in order to maximize the efficiency of the regime. First, the offer must be binding and credible, akin to a property right.[115] Incentives will be maximized if companies do not discount the financial reward *ex ante* for counterparty risk of breach. Second, it must be held open for decades to account for long time lags in pharmaceutical R&D. Third, the donor must foreswear the opportunity to purchase from a generic manufacturer during the period. The true innovator must be able to internalize the rewards.

c. Virtual IP Regimes: Innovation Sans TRIPS

It is also worthwhile to note what a donor purchase commitment does not entail. First, the offer need not be winner-take-all or rent-dissipating.[116] In normal pharmaceutical markets, multiple companies develop drugs for a particular condition, well aware of the competing research efforts. While the first to market with a patented product enjoys certain advantages, within short periods rival drugs are marketed, under different patents. The system need only distinguish between a free-rider generic (should not participate), a

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[114] Michael Kremer has carefully analyzed and articulated the donor purchase commitment model. Kremer, *supra* note 94, at 35-109. This paragraph is particularly indebted to his work.

[115] In a different context, several commentators have described binding negotiated market access commitments as property rights. Jose E. Alvarez, et al., *It's a Question of Market Access*, 96 Am. J. Int'l L. 56, 59 (2002).

[116] The classic works on the socially wasteful effects of patent races include Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J. L. & Econ. 265, 265-67 (1977) and Mark F. Grady & Jay I. Alexander, *Patent Law and Rent Dissipation*, 78 Va. L. Rev. 305, 305-10 (1992). In the context of drug prizes, it might be socially beneficial to have companies collectively spend more than the prize, as it would leverage the innovation effect of the prize. A $1 billion prize for an AIDS vaccine might stimulate $2 billion of R&D. This would be socially beneficial so long as the social benefits of an AIDS vaccine exceeded $2 billion.

near-simultaneous innovator (participates on a nearly equal basis),[117] and a me-too innovator (participates on a lesser basis).

This leads to the second point: distinguishing between these categories requires the donor to reference the patent law of some country (such as the US), but it does not require the target populations to have any IP laws at all. Strong IP laws under TRIPS are simply not required for this purpose. More broadly, any donor purchase commitment system does not require IP laws covering the target populations. The appropriate incentives are in place so long as the donor is bound to a credible commitment to acts *as if* they are bound by the IP laws of a reference country such as the US. This process creates a 'reference' or 'virtual' IP regime.

This is a significant point, not well understood or articulated by supporters of TRIPS implementation in low-income countries. Reference IP regimes will achieve all of the innovation advantages of TRIPS implementation in low-income countries, without the blocking effect of local IP laws. However, a more complex picture emerges when the scope is broadened from neglected disease drugs to global diseases such as AIDS.

2. Global Diseases: AIDS, Cardiovascular Disease, & Cancer

The neglected disease debate tends to overlook the fact that the chronic conditions of the high income and low income worlds are converging: cancer and cardiovascular disease are the second and third largest causes of death in developing countries.[118] Infectious diseases lacking a commercial market in the developing world receive increased market attention when they cross political borders into the OECD. AIDS is a global disease, bridging both worlds.[119] The category of *global diseases* presents unique innovation opportunities and challenges.[120]

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[117] Ron Winslow & David P. Hamilton, *Two Colorectal-Cancer Drugs are Near Approval*, Wall St. J., Feb. 12, 2004, at D5 (two innovative treatments for colorectal cancer are expected to receive FDA approval within 7 weeks of each other). It is unfair to label either drug as a me-too.

[118] World Health Organization, World Health Report 2003. Stephen Leeder, et al., A Race Against Time: The Challenge of Cardiovascular Disease in Developing Economies 12-15 (2004) ("In 1998, non-communicable diseases were responsible for 59% of total global mortality and 43% of the global burden of disease. Importantly, 78% of [non-communicable disease] deaths were borne by low- and middle-income countries, as was 85% of the NCD burden of disease…nearly 50% of deaths worldwide were due to CVD, diabetes, cancer and chronic lung disease."). PhRMA agrees with this position when it argues that the current 'Western oriented' R&D program actually includes diseases endemic to the entire world, such as cancer and CVD. Graham Dukes, UN Development Programme, Interim Report of Task Force 5 Working Group on Access to Essential Medicines App. 2, at 7-8 (Response of the Research-Based Pharmaceutical Industry to the Interim Report of the Task Force on Access to Essential Medicines) (Feb. 1, 2004).

[119] North America and Western Europe account for less than 2 million of the 34 to 46 million people living with HIV/AIDS in 2003. UNAIDS/WHO, AIDS Epidemic Update 37 (2003) [hereinafter UNAIDS/WHO, AIDS Epidemic Update]. While AIDS is a global disease, at least three global orphan drug market failures plague public health. One strain of AIDS (Type A) is largely confined to the developing world, and thus receives less research attention. Pediatric AIDS is also primarily a developing country issue. Nevirapine blocks the transmission of HIV to the infant during labor. Nevirapine is not widely distributed to the at risk population in low-income countries, resulting in unnecessarily high rates of pediatric transmission. UNAIDS/WHO, AIDS Epidemic Update, *supra* note 113, at 8-13 (noting the pediatric transmission of AIDS in Africa). In addition, formulations of most AIDS drugs are not well suited to

The most important fact about global diseases is that innovation is probably assured by the OECD markets alone. A few hundred thousand early AIDS cases in the US were sufficient to encourage pharmaceutical research companies to undertake aggressive research programs.[121] Likewise, aggressive research programs are underway in all of the chronic conditions endemic in the OECD, conditions which are now increasingly the cause of death in lower-income countries as well. With innovation assured, one would think that patent laws could stand aside and permit low-cost distribution for the poor. Once again, IP laws and the TRIPS Agreement loom large in the debate.[122]

Jean Lanjouw has made a novel proposal concerning pharmaceutical patents: requiring the innovator to choose patent protection in either rich countries, or poor countries, but not both.[123] If the condition is endemic in both rich and poor countries (or in just rich countries), the innovator will likely choose protection in rich countries. If the condition is unique to poor countries, her proposal would allow patent protection in that market. Restating her proposal in my framework: (1) tropical disease innovations should be patented only in poor countries; and (2) global disease innovations should be patented only in rich countries. The first proposition was critiqued in the section on neglected diseases immediately above.[124] The second proposition completely upends US policy on TRIPS, and returns most of the developing world to the pre-TRIPS environment. Indeed, the proposal can be reconciled with TRIPS only by greatly expanding the Doha and Cancun exceptions to include all global diseases. The developing world and essential medicine advocates would celebrate this result, but the US will never stand for it.

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children. Medecins sans Frontieres, Untangling the Web of Price Reductions: A Pricing Guide for the Purchase of ARVs for Developing Countries 5 (4th ed., 2003) [hereinafter MSF, Untangling the Web] ("Children living with HIV/AIDS are one of the most neglected populations: paediatric formulations are lacking and/or formulations do not meet children's and caregivers' needs (unpleasant tasting syrup, tablets too big to swallow, need to refrigerate some products, unbreakable tablets, lack of fixed dose combinations (FDCs), and non-adapted dosages. For example there are currently no fixed dose combinations for paediatric use").

[120] Herein, the term *global disease* refers to conditions for which a therapeutic market exists in the OECD, and the condition is also endemic to the developing world. The definition of global disease is not static. Malaria was once a global disease, but is now largely eradicated in the OECD. Increased international mobility is likely to further blur the epidemiological effect of political borders, encouraging R&D as global diseases migrate into the OECD. The eastward expansion of the EU is "importing" additional infectious disease threats into the EU, requiring enhanced public health responses to tuberculosis and AIDS. Richard J. Coker, Rifat A. Atun, & Martin McKee, *Health-care System Frailties and Public Health Control of Communicable Disease on the European Union's New Eastern Border*, 363 Lancet 1389-92 (Apr. 24, 2004). Likewise, migration from Latin America has suddenly exposed the US health care system to Chagas Disease. [cite]

[121] Indeed, many early AIDS drugs qualified for orphan drug status in the US, when the expected US market was fewer than 200,000 persons. Salbu, *supra* note 81, at 703-707.

[122] Correa interprets the Doha Declaration to include global diseases such as asthma and cancer. Correa, *Implications of Doha, supra* note 3, at 5. Others ask why diseases such as cancer and diabetes are not covered by Doha. Julian Fleet, *U.N. Approach to Access to Essential AIDS Medications, Intellectual Property Law and the WTO TRIPS Agreement*, 17 Emory Int'l L. J. 451, 465 (2003).

[123] Lanjouw, Global Diseases, *supra* note 92, at 5. Philipson and Mechoulan have criticized Lanjouw's proposal as providing an inadequate incentive for goods with strong positive externalities. Philipson & Mechoulan, *supra* note 59, at 19-20. This critique is misplaced, even if one assumes that global patent rents are sub-optimal at present. *See infra* Section IV.A.

[124] Section III.D.1 *supra.*

Politics aside, the practical challenge for the second proposal will be preventing the TRIPS-exempted poor nations of the world from exporting global disease generic medications to rich countries, the process of pharmaceutical arbitrage.[125] Despite these criticisms, Lanjouw's work importantly articulates the different markets which exist for pharmaceutical in rich and poor nations, and affirms that global disease innovation does not require IP laws in low-income nations.

3. The Public Domain and the Problem of Resistance

Once global disease patents expire, drug formulations enter the public domain.[126] After about fourteen years, all of the wonders of pharmaceutical innovation become freely available for world public health.[127] Perhaps a fourteen-year lag is a reasonable balance between cost, quality and access, particularly in global disease categories such as cancer, cardiovascular disease and other chronic conditions. Rich consumers pay for and receive the latest innovations (2004 medicine) while the poor might well be satisfied with the (slightly) less effective, but much less expensive, 1990 pharmacopoeia.[128]

This model might work in many situations, but it breaks down in the face of significant therapeutic advances. It may be acceptable to give the poor a slightly less effective but vastly cheaper drug. It is much more problematic to offer a grossly inferior treatment, or no treatment whatsoever. For example, the American Enterprise Institute alleges that ineffective off-patent malaria drugs are routinely provided to developing nations by global donors, while a patented effective drug is underutilized.[129]

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[125] Politics will again intrude on Lanjouw's proposal when the time comes to create the list of countries deemed poor enough to qualify for the exception. If the list is small (such as the 30 poorest countries permitted by the TRIPS Council to delay implementation), then generic AIDS ARVs would never reach South Africans or Brazilians. If the list is too large, then her assumption that the lost markets would be small would be false and R&D incentives would be weakened.

[126] The patent holder must first disclose the invention in a public filing. For a discussion of the disclosure norm in scientific research and patents, *see* Eisenberg, *Patents and the Progress of Science, supra* note 66; and Eisenberg, *Proprietary Rights, supra* note 66.

[127] Meaning available at the manufacturing cost, without the need for research cost recovery or royalty. This dynamic does not resolve the market failure of neglected drugs, which will never be developed absent adequate incentives.

[128] The Earth Institute's 2004 report adopts this position for cardio vascular medications because "multiple, cheap medications are now available. Pharmaceuticals in nearly every class of drug used for CVD are now off patent. There is no need to wait for a global trade agreement." Leeder et al., *supra* note , at 73-74. Lipitor would be a prominent counter-example. The report also highlights the marginal cost-effectiveness of some newer pharmaceuticals in resource-constrained settings. *Id.* At 74.

[129] Malarial resistance to chloroquine runs to 80% in some locations; an alternative drug, artemisinin, is more expensive and underutilized. AEI, Giving the Poor Drugs that Don't Work, (Dec. 2, 2003) *available at* www.aei.org. *But see* Jack C. Chow, M.D., Letter to the Editor, *WHO, Global Fund Get Best Medicine Available*, Wall. St. J., Jan. 26, 2004, at A15 (responding to the Jan. 21, 2004 editorial and the underlying article from Lancet).

Many diseases mutate in response to treatment. Antibiotics lose effectiveness as bacteria develop resistance.[130] ARV therapies lose effectiveness as the AIDS virus mutates.[131] Resistant strains of tuberculosis and malaria are increasingly evident.[132] Resistance is related to both usage and compliance. Resistance proceeds more quickly the more a drug is utilized and the less compliant patients are with the regime.[133] By the time the patent expires, the drug may be well on its way to ineffectiveness. In these cases, the public domain receives little of value. The poor get an ineffective drug, and perhaps nothing is in the pipeline to replace it if the condition no longer threatens OECD patients. The 'IP contract' has been breached.

One result of the biology of resistance is that certain pharmaceutical innovations lack the characteristic of inexhaustibility.[134] This calls for a major re-evaluation of pharmaceutical IP policy in this sub-field, treating some innovations as exhaustible resources which should be managed to optimize global public health.[135] Erik Kades has made a major step in that direction, suggesting that optimal management of antibiotics may require giving innovators much longer, or even perpetual patents.[136] Most of the literature on optimal patent length focuses on the innovation side of the equation; Kades' work redirects attention to the potential role of patents and NDRA law in rationalizing the utilization of exhaustible innovations. Establishing longer or perpetual patents for antibiotics would be a complete reversal of pre-Hatch-Waxman policy, which restricted special generic entry procedures to antibiotics.[137]

While Kades' suggested patent extension might resolve some of the issues created by exhaustibility, it has major implications for differential pricing and access for the poor.

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[130] A new class of antibiotics – fluoroquinolones – works well with drug resistant strains, but are expensive, leaving the poor with worn-out classes of antibiotics. Oxfam, *Fatal Side Effects: Medicine Patents Under the Microscope*, in Brigitte Granville, ed., The Economics of Essential Medicines 81, 93 (2002).

[131] Using cheaper ARVs rather than fixed dose combinations may hasten resistance. Marilyn Chase, *Drug to Curb Childbirth AIDS Spread Hits Hurdle*, Wall St. J., Feb. 10, 2004, at D4.

[132] Pecoul, et al., *supra* note 98, at 363-65 (specific examples of resistant strains in tropical diseases); AEI, Giving the Poor Drugs that Don't Work, (Dec. 2, 2003), *available at* www.aei.org.

[133] Disparities in compliance with treatment regimes may have many causes, including inadequate health care infrastructure, socio-economic factors, and cultural approaches to health.

[134] *See* Section III.A *supra* for a discussion of inexhaustibility.

[135] The economics of pricing exhaustible resources is discussed by Louis Philips, Philips, *supra* note 8, at ch. 7, including his interesting modification to Coase, *id.* at 125-29.

[136] Kades' argument is that public health would be maximized by granting long-term or perpetual patents for drugs which lose effectiveness with use, such as antibiotics. A patent holder rationally maximizes sales during the exclusive marketing period, even for uses which are medically marginal. From a public health perspective, this practice speeds the development of resistant strains of bacteria or viruses. Global public health would be maximized by extending the exclusive marketing period indefinitely, and encouraging judicious use of the drug in the most compelling cases. Eric A. Kades, Plagues and Patents (William & Mary Law School Working Paper No. 2003-Kades-1, Mar. 11, 2003) *available at* www.ssrn.com (No. 387241). Philipson and Mechoulan make a similar point when they conclude that the optimal patent life is infinite if the good creates negative externalities, giving antibiotic resistance as one example. Philipson & Mechoulan, *supra* note 59, at 9, 13-14.

[137] 21 U.S.C. § 357 (1996) (prior to amendment by Pub. L. No. 105-115, § 125(b)(1), 111 Stat. 2325 (1997)). While the Hatch-Waxman Act expanded the generic entry process to other drugs, 21 U.S.C. § 355(j) (2004), the special generic entry process for antibiotics was not repealed until 1997.

With an exhaustible resource, use should be 'managed' to maximize the social good (net positive externalities). If the market is chosen as the mechanism, and control given to the patent holder through an unlimited patent, exhaustible drugs will be rationed to the people most able to afford the increased price. Differential pricing for the poor is incompatible with the market allocation of exhaustible drugs.

One potential escape from this quandary is to choose a non-market method of allocation. For exhaustible drugs requiring management, a binding donor purchase commitment might be used to solve the supply side, while donor ownership and management could ration the demand queue with evidence-based medicine, preventing premature exhaustion. While Kades focuses on domestic management of the resource, the biology of resistance necessitates global management.

IV. The Heuristic of Globally Optimal Patent Rents

Assume that for any particular drug there is a *globally optimal patent rent*.[138] The globally optimal patent rent must be sufficient to recover research costs and fund future research. Optimization must balance concerns of cost, quality and access, looking for the greatest net gain to global public health. Maximizing R&D at all costs should not be the health policy goal. Some innovations are more valuable than others. Resources devoted to R&D are not available for other uses.[139] Companies allocate research funds in response to price signals from commercial pharmaceutical markets, which are largely unresponsive to the pervasive market failures described in Section III.D above.[140] For this reason Americans now have a third drug for erectile dysfunction,[141] and funds for

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[138] The economic analysis of socially optimal patents has been undertaken by Nordhaus and Scherer. Scherer, *Optimal Patent Life*, *supra* note 65, at 422; Nordhaus, *The Optimum Life of a Patent*, *supra* note 65, at 428; Nordhaus, *supra* note 59, at ch. 5. Scherer argues that shortening patent life will reduce R&D only for the most marginal inventions, particularly in industries with nonpatent barriers to entry and post innovation pricing discipline. Scherer, *Optimal Patent Life*, *supra,* at 426. The pharmaceutical research industry contains both conditions. Nordhaus concluded that a fixed patent life was not optimal, but given that requirement, the length of the life should err to a longer rather than a shorter period. Nordhaus, *The Optimum Life of a Patent*, *supra* at 428. Philipson and Mechoulan cover the same territory when they argue that "[a]ppropriate policy must *simultaneously* solve the externality problem ex-post and the R&D problem ex-ante." Philipson & Mechoulan, *supra* note 59, at 12-15. Recently, Christopher Yoo undertook a nuanced review of copyright law which covers some of the same terrain as my approach, but with assumptions of copyright market entry and substitutability which do not apply to pharmaceutical patents. See Christopher S. Yoo, *Copyright and Product Differentiation*, 79 N.Y.U.L. Rev. 212 (2004).

[139] Currently the US spends more than 15% of its GDP on health care. Stephen Heffler, et al., *Health Spending Projections Through 2013*, Health Affairs exh. 1 (Web Exclusive, Feb. 11, 2004) *available at* www.healthaffairs.org. Perhaps we can agree that increasing pharmaceutical R&D to 20% or 50% of GDP would be excessive.

[140] Philipson and Mechoulan make a similar point in the language of economics: "Under external effects in consumption, rewards to innovation should not be guided by potential *consumer* surplus, as under private goods, but the entire *social* surplus that includes benefits to non-consumers as well as consumers…" Philipson & Méchoulan, *supra* note 59, at 2.

[141] Viagra (sildenafil) was approved by the FDA in 1998, Levitra (vardenafil) in August 2003, and Cialis (tadalafil) in November 2003. *See* FDA Talk Paper, *FDA Approves Third Drug to Treat Erectile Dysfunction* (Nov. 21, 2003) *available at* http://www.fda.gov/bbs/topics/ANSWERS/2003/ANS01265.html; FDA Talk Paper, *FDA Approves New*

neglected disease innovation are literally going to the dogs,[142] but a malaria vaccine is not available.[143] The pharmaceutical industry currently spends more on sales and marketing than R&D.[144]

We can safely assume that the status quo rarely results in globally optimal patent rents. In a major recent study, the Congressional Budget Office conceded that no one knew whether current levels of pharmaceutical R&D were optimal.[145] And yet this is a pressing question. While it may be impossible to actually calculate globally optimal patent rents for the industry,[146] the concept is a useful heuristic to evaluate policy options.

A. Globally Sub-Optimal Patent Rents

Globally sub-optimal patent rents would stifle the production of innovative drugs, creating a generational equity issue. The present group of patients may benefit from sub-optimal patent rents because innovative treatments are cheaper and more available, but future quality will be compromised. Profit maximizing companies will not continue to cross-subsidize sub-optimal drugs with the profits from supra-optimal drugs: rather, sub-

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Drug for Treatment of Erectile Dysfunction in Men (Aug. 19, 2003) *available at* http://www.fda.gov/bbs/topics/ANSWERS/2003/ANS01249.html; and *First Oral Therapy for Erectile Dysfunction,* 28 FDA Medical Bull. 1 (Summer 1998) *available at* http://www.fda.gov/medbull/summer98/erectile.html.

[142] In 1999, the FDA approved two drugs to treat canine Cognitive Dysfunction Syndrome, also known as separation anxiety in dogs. FDA Talk Paper, *FDA Approves First Behavioral Drugs for Dogs* (Jan. 5, 1999) *available at* http://www.fda.gov/bbs/topics/answers/ans00934.html. Perhaps soon a drug will be developed for erectile dysfunction in dogs.

[143] For an introduction to donor efforts (led by the Bill & Melinda Gates Foundation) to stimulate development of a malaria vaccine, *see* http://www.malariavaccine.org.

[144] David H. Kreling, et al., The Kaiser Family Foundation, Prescription Drug Trends: A Chartbook Update exh. 30 (Nov. 2001) (top 10 major pharmaceutical manufactures in 2000 spent 34.4% of revenues on "marketing, general and administrative" and 13.7% on "research and development;" *but see* Uwe E. Reinhardt, *Perspectives on the Pharmaceutical Industry*, 20 Health Affairs 136 (2001) (not all SG&A expenses are truly marketing). With deference to Reinhardt, the differential is large enough to suggest that R&D receives less than marketing, absent more specific and verifiable data. Large marketing expenses are not proof that pharmaceutical patent rents are either supra- or sub-optimal, but merely indicate that the industry believes the return on investment in marketing is greater than alternative investments such as R&D.

[145] The 1998 study by the Congressional Budget Office states: "No one knows whether that amount of investment in R&D is over or under the optimal level." CBO, Increased Competition, *supra* note 28, at 48.

[146] The barriers to this calculation are both empirical and theoretical. On the empirical front, internal company data are not generally available to researchers. Studies by DiMasi, Hansen and Grabowski rely on self-reported company data rather than a truly objective data set. Joseph A. DiMasi, Ronald W. Hansen & Henry G. Grabowski, *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. of Health Economics 151 (2003). IRS data shows extraordinary profits and low taxation, Gary Guenther, Congressional Research Service, Federal Taxation of the Drug Industry from 1990 to 1996 (Dec. 13, 1999), but is protected against public disclosure by the Internal Revenue Code. Accurate pricing data is unavailable outside of the companies. CBO, Increased Competition, *supra* note 28, at 20. *See also* notes 140-144 *infra* and text accompanying. On the theoretical front, useful questions are posed by Reinhardt, *supra* note 135; and William S. Comanor, *Political Economy of the Pharmaceutical Industry*, 24 J. Econ. Lit. 1178, 1182-86 (1986).

optimal drugs will not be developed and profits from supra-optimal drugs will inure to shareholders and management.

B. Globally Supra-Optimal Patent Rents

Globally supra-optimal patent rents are rarely recognized as a problem by the pharmaceutical research companies. By definition, supra-optimal patent rents are not required to fund innovation. Supra-optimal patent rents result from excessive IP rights and DRA exclusive marketing periods, which needlessly delay the entry of innovation into the public domain.

Supra-optimal patent rents harm consumers by raising prices without the counterbalancing benefit of future innovation. Something more than consumer surplus is at stake here: excessive cost will inappropriately drive some patients to less effective alternative therapies, or away from medical treatment altogether.[147] Some scholars, including the anti-commons movement,[148] suggest that the neo-classical link between patents and innovation is overstated, particularly for industries marked by cumulative innovation.[149] If so, the optimal patent rent may be less than previously expected.

If global patent rents are sub-optimal, one would expect to see low or declining levels of R&D investment by the companies and constrained profits. In fact, R&D spending is growing,[150] and the pharmaceutical research companies lead the markets in spending on R&D.[151] The industry's long-term profits are four times the rate of the Fortune 500.[152] Analysis of IRS data from 1990 to 1996 demonstrates that the drug industry's after-tax profits are more than triple the rate for all industries. Their effective federal income tax rate is 16.2%, compared with 27.3% generally.[153] It certainly seems plausible that supra-optimal patent rents are currently being collected.

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[147] The mechanisms for reduced access may vary. If a patient is unable to afford all of the prescriptions, they may be forced to choose which ones they buy and which ones they forego. Others may take their medications on a less frequent basis, reducing the average daily cost, but with potentially dangerous effects on safety and efficacy. Third-party payors erect managed care barriers to reduce the utilization of expensive drugs.

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

[149] Oren Bar-Gill & Gideon Parchomovsky, *The Value of Giving Away Secrets*, 89 Va. L. Rev. 1857 (2003). While Bar-Gill and Parchomovsky list "pharmacology" as one such industry, they do not make that case convincingly in the article. If pharmaceutical research companies are eager to publish and forego patents, it is a nascent trend.

[150] During the decade 1990 to 2000, pharmaceutical research companies reported increased levels of R&D, Kreling, *supra* note 135, at exh. 31.

[151] Pharmaceutical research companies spent in excess of $47 billion on R&D in 2002. European Federation of Pharmaceutical Industries and Associations, The Pharmaceutical Industry in Figures, 2003 Update (2003).

[152] Kreling, *supra* note 135, at exh. 32. The judgment of the equity markets is significant, even under a weak form of the efficient capital markets hypothesis.

[153] Guenther, *supra* note 137.

C. Implications of Global Optimality

Absent confidential pharmaceutical research company data,[154] no one knows whether current levels of R&D are optimal or not. No matter how that issue is ultimately resolved, the concept of globally optimal patent rents is useful as a heuristic tool.[155] The following section outlines several implications which follow from the discussion to this point, even in the absence of empirical data on optimality.

1. Differential Pricing

Patented pharmaceuticals can be delivered at marginal cost of production to the poor without harming innovation. For example, the vast majority of AIDS patients in developing countries are quite poor and are not part of the global market for patented drugs. Supplying their needs is a humanitarian response, with no markets actually lost to the pharmaceutical companies. These non-market patients could receive unlicensed or royalty-free drugs without impacting the cash flow of pharmaceutical research companies.[156]

If global patent rents are already sub-optimal, royalty-free production should still be allowed so long as it did not replace any commercial market, and thus did no financial harm to the patent owner.[157] Monitoring costs would be borne by third parties in order to prevent additional expense to the innovator. If global patent rents are already supra-optimal, pharmaceutical research companies could bear the expenses of monitoring and enforcing differential pricing without harming innovation.

Supra-optimality also permits expansion of differential pricing programs to middle-income countries, even with some displacement of commercial markets. The magnitude

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[154] A major barrier to global optimization is the lack of public data on both R&D and research cost recovery by these companies. Pharmaceutical pricing data is notoriously opaque and misleading. Schneider, *supra* note 33; Gardiner Harris, *Drug Companies Settle 7 Suits for $1.6 Billion*, N.Y. Times, Nov. 6, 2003 ("Drug companies have paid a total of $1.6 billion since 2001 to settle seven suits brought by whistle-blowers that accused them of marketing fraud and overbilling Medicare and Medicaid"). Some researchers suggest that increased pricing opacity is necessary to sustain differential pricing for low-income countries. Patricia M. Danzon & Adrian Towse, Differential Pricing for Pharmaceuticals: Reconciling Access, R&D and Patents 16-20 (AEI-Brookings Joint Center for Regulatory Studies, Working Paper 03-7, July 2003).

[155] Given the above average returns in this sector, it may be presumed that supra-optimal patent rents are being earned on essential access medications. The burden of coming forward with contrary evidence could be placed on the parties controlling the relevant information, the pharmaceutical research companies.

[156] This topic is explored in depth in Section V *infra*.

[157] Philipson and Mechoulan criticize this position, but their stance is undermined if global patent rents are supra-optimal. Philipson & Mechoulan, *supra* note 59, at 19-20. Even if one assumes sub-optimality, differential pricing for ARVs does not reduce R&D incentives if cash flows to the innovators are untouched. Philipson and Mechoulan's argument thus collapses to a complaint that differential pricing does not improve upon status quo R&D incentives. If the effect in innovation is positive or neutral, the health gains (positive externalities) from increased access should drive policy.

of expense and market loss that could be tolerated would depend on the amount by which patent rents were supra-optimal.[158]

2. Compulsory Licensing

For developing countries, compulsory licensing may be required. Compulsory licensing creates a credible threat on the part of low- and medium-income countries, pressuring pharmaceutical research companies to undertake the hazards of differential pricing. US threats of compulsory licensing of ciprofloxacin were instrumental in securing a lower price from Bayer,[159] and remains an important remedy in litigation.[160] Brazilian compulsory licenses permitted the distribution of free ARVs to any Brazilian with AIDS.[161] Medicines Sans Frontieres and others consider the threat and use of compulsory licenses to have been essential in convincing companies to establish meaningful differential pricing programs.[162]

A free rider problem emerges if compulsory licensure is evaluated at the national level. Each country may rationally choose to shirk its share of R&D costs, the same free rider problem afflicting innovation generally. The decision to compel a license requires some form of global coordination to internalize the negative externality. The TRIPS modifications at Doha and Cancun are prominent intermediate steps, limiting compulsory

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[158] Pharmaceutical company data problems are also faced in estimating arbitrage losses. In its 2001 submission to the United States Trade Representative, PhRMA claimed that $260 million was lost annually due to unlicensed drug products in Argentina. Pharmaceutical Research Manufacturers of America, National Trade Estimate Report on Foreign Trade Barriers (NTE) (Dec. 17, 2001) *cited in* Susan K. Sell, *TRIPS and the Access to Medicines Campaign*, 20 Wisc. Int'l L. J. 481, n.55 (2002) [hereinafter Sell, *TRIPS*]. In 2003, the estimate has ballooned to $600 million, without any apparent verification. United States Office of Trade Representative, 2003 National Trade Estimate Report on Foreign Trade Barriers 5-6 (2003) *available at* www.ustr.gov/reports/nte/2003/index.htm.

[159] Jill Carroll & Ron Winslow, *Bayer Agrees to Slash Prices for Cipro Drug*, Wall Street Journal, Oct. 25, 2001 ("The agreement comes after a high-stakes threat by Tommy Thompson, HHS secretary, to break Bayer's patent for Cipro if he didn't get the price he wanted."). The US compulsory license statutes are 7 U.S.C. § 2404 (patents necessary for the nation's food supply), 17 U.S.C. § 115 (2004) (copyrights to certain musical works), 28 U.S.C. § 1498 (2004) (patents); 35 U.S.C. § 203 (patents developed through the use of government research funding under the Bayh-Dole Act); and 42 U.S.C. § 2183 (atomic energy). The US compulsory license statutes do not contain the restrictions required by Article 31 of TRIPS. *See* TRIPS Agreement, *supra* note 2, at art. 31. In May 2004, the US held a Bayh-Dole hearing on the compulsory licensure of an AIDS drug. [cite to Fed Reg].

[160] Makan Delrahim, Deputy Assistant Attorney General, Antitrust Division, *Forcing Firms To Share the Sandbox: Compulsory Licensing of Intellectual Property Rights and Antitrust*, Presentation at the British Institute of International and Comparative Law, May 10, 2004.

[161] Jorge Bermudez, *Expanding Access to Essential Medicines in Brazil: Recent Economic Regulation, Policy-Making and Lessons Learnt*, *in* Brigitte Granville, The Economics of Essential Medicines 193 (2002); *see also* Judy Rein, *International Governance Through Trade Agreements: Patent Protection for Essential Medicines,* 21 Northwestern J. Int'l L. & Bus. 379, 394-404 (2001) (resistance by Brazil, South Africa and Thailand).

[162] World Health Organization, Surmounting Challenges: Procurement of Antiretroviral Medicines in Low- and Middle-Income Countries: The Experience of Medicins Sans Frontieres 7 (pre-publication draft, 2003) [hereinafter WHO, Surmounting Challenges]; Marleen Boelaert, et al., *Letter to the Editor*, 287 J. Am. Medical Ass'n 840-41 (2002) ("This impressive discount offered by the companies to developing countries was not merely due to public outcry, but mostly as a response to competition by generic drugs").

licensure to those nations with the greatest need, and attempting to limit the negative externalities which might flow from pharmaceutical arbitrage of products produced under compulsory license.[163]

Compulsory licenses for non-commercial markets will not harm innovation if arbitrage is blocked. Royalty-free production by a third party does not add any marginal cost to the innovator, and thus will not harm innovation in this case.[164] If global patent rents are supra-optimal, then royalty levels on compulsory licenses may be zero without loss of innovation incentives. The burden of proof of sub-optimality should be on the innovator companies seeking a higher royalty, and the royalty rate in conditions of sub-optimality should balance innovation and access goals.

3. Pharmaceutical Arbitrage

The case for restricting pharmaceutical arbitrage is strongest for exports from targeted non-commercial markets into OECD markets.[165] This arbitrage undermines differential pricing and compulsory licenses for the poor, particularly if global patent rents are sub-optimal. The EU recognizes that its attempts to support differential pricing for essential medicines depend upon blocking arbitrage into the OECD.[166]

It is important to note the limited scope of the case against pharmaceutical arbitrage. For example, it does not apply to generic drugs. For generic drugs, increasing the generic company's profits will not incentivize innovative R&D, and thus arbitrage restrictions on generic drugs are not supportable on innovation grounds.[167] Restrictions are also inappropriate between and to low-income nations, so long as commercial markets are not replaced. Restrictions are also unnecessary between OECD nations if patent rents are supra-optimal. Put another way, parallel trade in patented pharmaceuticals within the OECD does not harm innovation so long as patent rents remain supra-optimal.[168] Pharmaceutical arbitrage within the OECD is the subject of the second case study on Canadian-US pharmaceutical arbitrage.

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[163] For a description of these modifications, *see* Section V.C *infra*.

[164] Assuming that production for compulsory licensure is limited to non-commercial markets. This result holds without regard for whether patent rents are currently super- or sub-optimal. Critiques of compulsory licenses by Merges and others are not applicable here because the goal is not the initiation of efficient bargaining around a rule, but the provision of essential medicines at marginal cost without harming innovation. *See* Robert P. Merges, *Contracting into Liability Rules: Intellectual Property Rights and Collective Rights Organizations*, 84 Calif. L. Rev. 1293 (1996) (arguing that compulsory licenses in digital media are less efficient than private contractual efforts).

[165] *See supra* note 97 for a definition of the term *OECD markets*.

[166] DG Trade, *supra* note 7, at §1.

[167] Restrictions might be appropriate on other grounds, such as safety.

[168] Parallel trade from poor countries to rich countries is incompatible with differential pricing of essential medicines. *See* Danzon & Towse, *supra* note 145 (parallel trade defeats the objectives of differential pricing); and David A. Malueg & Marius Schwartz, *Parallel Imports, Demand Dispersion, and International Price Discrimination*, 37 J. Int'l Economics 167, 193 (1994). For unpatented or generic products, no innovation-based case for banning parallel trade can be offered.

If patent rents are sub-optimal, the domestic exhaustion rule could apply in OECD markets, forbidding parallel imports into OECD countries and raising patent rents. Otherwise, the international exhaustion rule should apply to sales between OECD markets since consumers will benefit while innovation incentives remain intact. Outside of OECD markets, the international exhaustion rule should always be applied, as there is no innovation-based warrant for denying access to the poor.

4. Push and Pull Subsidies

Another form of optimization creates subsidies to achieve particular goals. Subsidies for pharmaceutical innovation may be divided between *push* and *pull*. Push subsidies include tax credits for R&D, general research grants such as the US National Institutes of Health,[169] and the orphan drug tax credit.[170] Pull subsidies include the patent system and donor purchase commitments for development of a specific pharmaceutical, such as an AIDS or malaria vaccine[171] or antidotes to bioterrorism.[172]

Optimization implies three conclusions: (1) For drugs or conditions with sub-optimal patent rents, government intervention should increase patent rents towards optimal levels. For example, subsidies are essential for neglected disease conditions, where the target population cannot afford any commercial price for therapy; (2) Subsidies can be limited to drugs with sub-optimal patent rents without harming innovation. Scarce subsidies should not be directed to drugs with strong commercial potential, but should be reserved for neglected diseases; and (3) For patented drugs with supra-optimal patent rents, the government may intervene to achieve other goals, such as improved financial access, without undermining R&D innovation.

5. National Drug Regulation

National regimes for testing the safety and efficacy of patented drugs are inefficient, duplicating scientific work and wasting resources unnecessarily. Each New Chemical

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[169] Public funding of basic research remains robust, but public funding is not available in the amounts necessary to completely replace private R&D. In any event, public funding of all pharmaceutical R&D would be the equivalent of nationalizing the pharmaceutical industry's research program, with many collateral results. The case is strongest for public or donor funding of neglected drugs. Current examples include tuberculosis, *see* The Global Alliance for TB Drug Development, available at www.tballiance.org, and for a vaccine for malaria, *see* http://www.malariavaccine.org.

[170] Hsu and Schwartz, *supra* note 94, at 43-45. By contrast, the exclusive marketing period under the Orphan Drug Act is a pull subsidy. Scherer and Watal have proposed expanding US tax incentives for donating pharmaceuticals to poor nations, Frederick M. Scherer & Jayashree Watal, *Post-TRIPS Options For Access to Patented Medicines for Developing Countries* (WHO Commission on Macroeconomics and Health, 2001) [hereinafter Scherer & Watal, *Post-TRIPS Options*], but this additional push subsidy is warranted only if patent rents are sub-optimal.

[171] Michael Kremer, *Pharmaceuticals and the Developing World*, 16 J. of Econ. Persp. 67, 82-85 (2002); Kremer, *supra* note 94.

[172] The Congressional Research Service indicates that "guaranteeing a market through contract authority" is an aspect of President Bush's Project BioShield to develop bioterror countermeasures. Frank Gottron, Project Bioshield (CRS Report for Congress, RS21507) (July 23, 2003). The proposed size of the pull subsidy for bioterror countermeasures is $5.593 billion through FY 2013. *Id.*

Entity (NCE) requires clearance by the FDA in the US and parallel regulatory authorities throughout the OECD,[173] as well as by the DRA in every nation where the drug will be sold. Some estimates put the cost of duplicative DRA processes within the EU alone at £500 million per year,[174] which is enough to support the development of three new patented drugs.[175] DRA rules also delay the launch of innovative drugs in many countries.[176] A 'reference' approval process would reduce duplicative costs and speed market entry of pharmaceuticals.[177]

Resources are also wasted in the generic entry process. DRAs should not require generic applicants to repeat clinical studies without a clear benefit to public health.[178] Generic companies operating under a compulsory license expend resources to reverse engineer patented drugs. Reverse engineering in this case is a wasteful effort and delays launch in low-income countries by several years.[179]

Reducing these costs makes R&D more productive, lowers the threshold for cost-effective innovation, and delivers innovative drugs to patients more quickly. Innovators will collect more revenue when patented drugs gain marketing approval more quickly.[180]

6. Price Controls

This article is agnostic on the question of the desirability of pharmaceutical price controls generally;[181] the purpose of this section is to describe what form price controls should (or should not) take if policy makers choose to adopt them.

The concept of globally optimal patent rents suggests six conclusions about pharmaceutical price controls: (1) Price controls should exclude generic products; (2)

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[173] One attempt at coordination is the European Agency for the Evaluation of Medicinal Products (EMEA). Council Regulation 2309/93, O.J. (L 214) as amended by Commission Regulation 649/98 O.J. (L 88) 7.

[174] Rothnie, *supra* note 43, at 493-94 and sources cited therein.

[175] Assuming a market of $250 million per year is required to support development of a new drug, *see supra* note 94, and an exchange rate of 1.5 US dollars to the English pound.

[176] *See* Patricia M. Danzon, Y. Richard Wang & Liang Wang, *Impact of Price Regulation on the Launch Delay of New Drugs: Evidence From Twenty-Five Major Markets in the 1990s* (Nat'l Bureau of Econ. Research, Working Paper No. 9874, July 2003). This study collects data on launch delay, and concludes that in addition to difficulties with the drug approval process, many companies delay applications to enter some smaller markets due to fears of pharmaceutical arbitrage. If global patent rents are supra-optimal, this industry practice is reprehensible, as it voluntarily withholds important drugs from patients.

[177] *See infra* Section V.F.2 and notes accompanying.

[178] Pharmaceutical research companies withhold much of this data as trade secrets, but when a patent is set to expire, there is no innovation warrant to delay generic entry, unless all generic entry is premature.

[179] Watal reports a lag of about two years for unlicensed pharmaceuticals reverse-engineered in India. Jayashree Watal, *Pharmaceutical Patents, Prices and Welfare Losses: A Simulation Study of Policy Options for India under the WTO TRIPS Agreement,* 23 The World Economy 733-52 (2000).

[180] As Danzon, Wang & Wang observe, the companies will also want protection against pharmaceutical arbitrage. Danzon, et al., *supra* note 165.

[181] In the EU, pharmaceutical prices are generally constrained by government action. DG Trade, *supra* note 7, at § 3.3; Rothnie, *supra* note 43, at 487-94. Any price control process would be vulnerable to manipulation and lobbying, Lanjouw, Global Diseases, *supra* note 92, as well as the many other inefficiencies of price controls generally.

Rate-setting is preferred over price-fixing; (3) Developing country prices should not be used in OECD external reference pricing systems; (4) Rate-setting should be stable over long periods of time, giving companies accurate *ex ante* innovation incentives; (5) Optimization requires access to pharmaceutical research company data on a global basis; and (6) Optimization requires governments to account for the external (international) effects of national-level pricing controls. Creative destruction of the current OECD cost-shifting patterns could realign prices appropriately.

First, generic pharmaceutical products must be excluded from price controls. The special case for government intervention in pharmaceutical prices derives from the monopoly market power granted by the state for patented drugs. Generic products do not generate monopoly rents, and thus should be exempt.[182]

Second, optimizing patent rents requires rate-setting rather than price-fixing and reference pricing. Price-fixing implies a price level without special regard to the innovator company's return on investment. Likewise, reference pricing proceeds without considering issues of optimizing innovation. If the goal is optimization, some form of rate-setting is required.[183]

Third, differential pricing for the poor requires blocking actual arbitrage from low- and medium-income countries into OECD markets.[184] Likewise, virtual forms of this arbitrage must be prevented. OECD markets should not utilize developing country prices as an external reference price within the OECD.[185]

Fourth, price controls must be stable over long periods of time. Pharmaceutical research requires long lead times before marketing. Companies should receive accurate *ex ante* pricing signals that are reliable. Otherwise, companies will discount the current price

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[182] Internal reference pricing systems should refer to generic prices within the therapeutic class, but generics themselves should not be reimbursed under an internal reference pricing system. Inclusion is not warranted, and may actually keep the generic prices artificially high. No pro-innovation goal is served by artificially high generic prices, other than a very indirect and inefficient subsidy of the innovator companies.

[183] I use the term 'rate-setting' very broadly here, not limited to the model of utility rate-setting. For example, I consider the Hatch-Waxman Act to be a form of rate-setting, balancing the goals of innovation and low-cost access. Modifications to the doctrine of patent breadth, or extending the length of patents would have similar effect, if the goal was to optimize the balance between cost, quality and access. *See* Merges & Nelson, *supra* note 65.

[184] *See* Section IV.C.3 *supra*.

[185] F.M. Scherer & Jayashree Watal, *The Economics of TRIPS Options for Access to Medicines*, *in* Brigitte Granville, ed., The Economics of Essential Medicines, 32, 48-49 (2002) (arguing for a ban on external reference pricing which uses prices in low-income nations). Just as physical arbitrage, this practice should be restricted only when it flows from poor to rich nations. External reference pricing within the OECD, or within low- and middle-income countries does not undermine differential pricing for the poor. *But see* Scherer & Watal, *supra*, at 49 (also suggesting preventing parallel exports from any price-controlled country). Danzon and Towse address the external reference pricing problem by suggesting increased pricing obscurity and opacity so that the rock-bottom prices are not "directly observable." Danzon & Towse, *supra* note 145, at 6, 16-17. Their solution is vigorously rejected by Medicins Sans Frontieres, which has been very active in negotiations price discounts and distributing ARVs in sub-Saharan Africa. MSF, Untangling the Web, *supra* note 113; WHO, Surmounting Challenges, *supra* note 113, at 7.

signals from an expected market for the political risk of more onerous price controls, increasing the scope of the market failures discussed in Section III.D *supra*.

Fifth, optimizing patent rents on a national basis makes no sense. Pharmaceutical R&D is a global business, and any attempts to calculate optimal patent rents on a national basis invites both free riders and transfer pricing games on a grand scale. Optimization requires accurate data on pharmaceutical pricing, profitability, and innovation. This information is not currently available to independent researchers.

Sixth, government price controls frequently fail to account for negative externalities. For example, if the EU sets patented drug prices quite low,[186] pharmaceutical research companies will attempt to recover their R&D investments by raising prices in uncontrolled markets. The US is the largest such market,[187] meaning that price controls in Europe shift R&D costs to the US market, raising US drug prices.[188] Any action which significantly reduces US drug prices will destabilize the current system. Pharmaceutical research companies and OECD governments will have to renegotiate national or global pricing strategies.[189] The AIDS crisis created the essential access movement which led to Doha and Cancun. Creative destruction of the OECD internal differential pricing system could generate political change. The burden of innovation should be shared equitably amongst wealthy consumers, not disproportionately subsidized by the people of the United States.

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In Part Two of this article, pharmaceutical arbitrage will now be examined in two major public health issues: the AIDS crisis in sub-Saharan Africa, and prescription drug re-importation from Canada to the US. In both cases, pharmaceutical arbitrage entails major implications. In the case of sub-Saharan AIDS, certain forms of arbitrage are inappropriate, specifically exports from sub-Saharan nations to the OECD of differentially priced ARVs. Unfortunately, both TRIPS and the US government are attempting to impose far greater restrictions in the name of innovation, with serious public health implications. In the Canadian-US pharmaceutical arbitrage case study, the

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[186] DG Trade, *supra* note 7, at § 3.3 ("In the EC, patented pharmaceutical products are different from other patented products in the sense that there is no free market. National policies keep healthcare services and reimbursement schemes for medicines tightly controlled").

[187] The United States did not adopt price controls on pharmaceuticals in the recently-enacted Medicare drug benefit. Prescription Drug and Medicare Improvement Act of 2003, Pub. L. No. 108-173, § 301, 42 U.S.C. §§ 1395 et seq. [§ 1808(c)(1)(C) of the SSA] (2004). However, the United States is not entirely immune to rate-setting inclinations in health care. Almost every other major health care good or service purchased by Medicare or Medicaid is subject to rate-setting, including the services of physicians, hospitals, ambulatory surgical centers, and home health agencies. For a discussion of Medicare and Medicaid pharmaceutical pricing options, see Schneider, *supra* note 33, at 20-22, 45-48.

[188] The data demonstrates both increased R&D spending, Kreling, *supra* note 135, at exh. 31, and increased US drug prices. NIHCM Foundation, Prescription Drug Expenditures in 2001: Another Year of Escalating Costs 9 (Rev. ed., 2002) [hereinafter, NIHCM Foundation, Prescription Drug Expenditures].

[189] The USTR is currently using free trade agreement negotiations to induce nations such as Australia to modify its domestic pricing systems for pharmaceuticals. Elizabeth Becker, *Drug Industry Seeks to Sway Prices Overseas*, N.Y. Times, Nov. 27, 2003.

desirability of the practice hinges on whether global patent rents are supra-optimal or not, and whether one credits the fears on safety of Canadian sourced drugs. If global patent rents are supra-optimal and safety concerns overblown, then US consumers are needlessly overcharged for patented drugs, and many suffer negative health outcomes from restricted access. In both case studies, state interventions in pharmaceutical arbitrage are uncoordinated, often counterproductive, and frequently uninformed by appropriate theory.

PART TWO. THE PRAXIS OF PHARMACEUTICAL ARBITRAGE: TWO CASE STUDIES

V. Pharmaceutical Arbitrage and AIDS in Sub-Saharan Africa

The following case study on AIDS highlights the reluctance of pharmaceutical research companies to make patented ARV drugs available on an affordable basis. Fear of pharmaceutical arbitrage and the general weakening of IP laws are the root causes of this reluctance. Government intervention in support of differential pricing for global diseases thus has the potential to transcend the competing goals of innovation and financial access, by improving access while supporting optimal R&D.

A. Financial Constraints Limit Access to AIDS Drugs in sub-Saharan Africa

Globally, AIDS is not under control, with approximately 40 million persons living with HIV/AIDS worldwide.[190] Ninety-five percent live outside of North America and Western Europe. Two thirds of infected persons, new infections and deaths are in sub-Saharan Africa.[191] An estimated 5.5 million people in developing countries need ARV treatment for HIV/AIDS, but only 5% of those currently receive it; in sub-Saharan Africa in 2003, only 1% of the people who need ARV therapy actually receive it.[192]

Purchasing AIDS drugs at US prices is not an option for the vast majority of these people. The per capita annual cost of a popular ARV in the US is $6894,[193] and the recently introduced Fuzeon (enfuvirtide) costs $20,000 per year.[194] The annual per capita

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[190] UNAIDS/WHO, AIDS Epidemic Update, *supra* note 113, at 2. While much progress has been made, AIDS is not fully under control in the OECD. In 2003, 66,000 to 94,000 persons were newly infected with HIV in North America and Western Europe. *Id.* at 38. But these numbers are quite small when compared to sub-Saharan Africa, and the health and longevity of the US patients have improved. *Id.* at 28-30 ("AIDS mortality continues to drop, thanks to the widespread availability of antiretroviral treatment").

[191] UNAIDS/WHO, AIDS Epidemic Update, *supra* note 113, at 38; Robert Greener, UNAIDS, *HIV/AIDS and Absorptive Capacity* (Kaiser Family Foundation HealthCast, Jan. 29, 2004) (2003 data) *available at* http://www.kaisernetwork.org/health_cast/hcast_index.cfm?display=detail&hc=1066 [hereinafter Greener, UNAIDS].

[192] In sub-Saharan Africa, less than 1% currently receive ARV treatment. WHO, Surmounting Challenges, *supra* note 152, at 2, 5. Reuters, *UN to Seek $6 Billion to Fight AIDS in Third World*, Nov. 6, 2003.

[193] In the US, the annual cost for Combivir is $6894, as described in Section V.A.1 *infra*.

[194] Vanessa Fuhrmans, *Medical Dilemma: Costly New Drug for AIDS Means Some Go Without; Programs for the Uninsured are Facing Tough Choices With Advent of Fuzeon,* Wall St. J., Jan. 13, 2004. Fuzeon is the first fusion inhibitor treatment for HIV, developed at Duke University. Ironically, high cost has forced the North Carolina AIDS assistance project to strictly ration the number of residents who can receive the

health expenditures in sub-Saharan Africa averages $31.10[195] and range from $12 (Malawi) to $253 (South Africa).[196] Reducing the price of AIDS medications for the poor is thus a necessary condition to extending ARV treatments to millions of afflicted persons worldwide.[197] Recognizing the important public health issues, Brazil,[198] India,[199] South Africa,[200] and China[201] produce unlicensed ARVs for the poor, provoking conflicts between human rights and IP rights. Differential pricing and compulsory licenses are key components in this conflict. The European Commission's mandate is to "pursue tiered [differential] pricing as the principal means of rendering essential medicines affordable … to the poorest populations."[202]

1. Differential Pricing of ARVs

Most patented drugs can be produced relatively cheaply, absent research cost recovery. The primary variable expenses are direct manufacturing costs, which are a small fraction of the retail prices of patented ARVs.[203] A high ratio of retail prices to direct manufacturing costs enables a company to sell at highly differentiated prices without

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treatment. U-Wire, Duke University: North Carolina Firm's New AIDS Drug Development On Hold, 2004 WL 59460572 (Jan. 22, 2004) ("Steve Sherman, director of North Carolina's ADAP, said the program set a cap for 25 state residents to be eligible for Fuzeon treatment at any one time, creating a system of rationing medical care.") Other states such as Alabama have decided the cost is too high to cover the drug at all, despite its effectiveness. Fuhrmans, *supra*.

[195] World Bank, 2004 World Development Indicators (2001 data).

[196] World Bank, 2004 World Development Indicators (2001 data); *see also* Markus Haacker, *Providing Health Care to HIV Patients in Southern Africa,* in Brigitte Granville, ed., The Economics of Essential Medicines, 242, 244 (2002). After adjustments for purchasing power parity, Haacker's figures rise to $44.8 (Malawi) and $552.3 (South Africa).

[197] Funds for ARVs and drugs to treat opportunistic infections are scarce. UNAIDS estimates these needs at approximately 37% of the total $10.7 billion which should be spent on HIV/AIDS in 2005 for a comprehensive response. Total unmet financial need in 2005 is projected at approximately $5 billion. Greener, UNAIDS, *supra* note 180. If these drugs were available at a much lower cost, resources could be redeployed to prevention and other unmet priorities.

[198] Ellen 't Hoen, *TRIPS, Pharmaceutical Patents, and Access to Essential Medicines: A Long Way from Seattle to Doha,* 3 Chi. J. Int'l L. 27, 32-33 (2002) [hereinafter 't Hoen, *TRIPS*].

[199] Mark Schoofs, *Clinton Program Would Help Poor Nations Get AIDS Drugs*, Wall St. J., Oct. 23, 2003, at B1 (Indian and South African drug companies); Cipla 2002-2003 Annual Report, *supra* note 106, at 7 ("In HIV/AIDS care, the Company continued its pioneering role in making available a range of antiretroviral drugs including unique combination products. These were made available at reasonable prices not only in India but also in other parts of the world").

[200] Schoofs, *supra* note 187, at B1 (Indian and South African drug companies); 't Hoen, *TRIPS, supra* note 186, at 30-31 (describing South Africa's efforts to provide royalty-free ARVs to its population and the legal and political challenges to those actions by the United States and pharmaceutical research companies).

[201] Jim Yardley, *China Begins Giving Free H.I.V./AIDS Drugs to the Poor*, N.Y. Times, Nov. 8, 2003 *available at* www.nytimes.com.

[202] DG Trade, *supra* note 7, at §2.2. Low-income countries targeted for essential medications by the EU had a per capita income of less than $765 in 2000.

[203] Other costs include diagnosis, ongoing non-pharmaceutical treatment and related infrastructure requirements. While these costs and infrastructure barriers are significant, the key variable in many diseases is the affordability of the prescription medication.

selling below marginal cost.[204] Differential pricing ratios currently exceed 30:1 in ARV drugs. For example, in November 2003, a daily dose of GlaxoSmithKline's best selling combination ARV drug Combivir[205] costs about $18.89 per day or $6895 per year by mail order in the United States.[206] In sub-Saharan Africa in 2003, GlaxoSmithKline sells Combivir to health agencies at 90 cents per day or $329 per year.[207] At the same time, Aurobindo of Hyderabad, India sells an unlicensed form of Combivir to governments and nonprofit agencies at 56 cents per day or $204 per year. Medecins sans Frontieres targets an annual per patient cost of $50 to $100 in the near future.[208] These price reductions are important, since the per capita income in 24 low-income countries is less than $2.10 per day.[209]

2. ARV Arbitrage

Significant differential pricing in ARV drugs, combined with the poverty of the intended recipients of the drugs creates significant arbitrage pressure.[210] A kilogram of the active ingredients in Combivir™ is about a 3 year supply, worth about $20,000 in the US, but selling for as little as $612 in Hyderabad and sub-Saharan Africa.[211] This arbitrage differential is equal to about 25 times the average per capita income in 24 low-income countries. Entrepreneurs[212] will divert these drugs from the poor and export them to

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[204] Alan Sager & Deborah Socolar, Do Drug Makers Lose Money on Canadian Imports? 7 (Boston University Health Reform Program, Data Brief No. 6, Apr. 15, 2004) (roughly estimating marginal US manufacturing and distribution costs for prescription drugs to be 9.9%).

[205] Combivir is a fixed dose combination (FDC) of 300 mg zidovudin (ZDV or AZT) and 150 mg of lamivudine (3TC). MSF, Untangling the Web, *supra* note 113, at 13.

[206]Calculation of the US price comes from drugstore.com (180 tablets of Combivir for $1,699.99, taken twice per day), *available at* www.drugstore.com (visited Nov. 8, 2003).

[206] 't Hoen, *TRIPS, supra,* note 186, at 32-33.

[207] MSF, Untangling the Web, *supra* note 113, at 13.

[208] WHO, Surmounting Challenges, *supra* note 152, at 9. As of 2004, the WHO 3 x 5 program estimates the per person per year cost for first-line drugs at US$304. World Health Organization, The World Health Report 2004: Changing History 30 (2004).

[209] DG Trade, *supra* note 7, at §2.2. It is important to note that the price charged to governments is not the same as the retail price to patients, which can increase due to markups, or decline with charitable subsidies. For example, a common triple FDC AIDS drug (lamivudine-stavudine-nevirapine) is listed in the Pricing Guide as selling to agencies for as little as 77 cents per day, MSF, Untangling the Web, *supra* note 113, at 13, but media reports indicate a consumer price in sub-Saharan Africa of 55 cents per day, declining soon to 36 cents per day under a deal brokered by the Clinton Foundation. Schoofs, *supra* note 187, at B1; Press Release, Medecins sans Frontieres, *AIDS Drugs Now Available for 36 US Cents a Day Under Clinton Foundation Deal* (Oct. 23, 2003) *available at* www.accessmed-msf.org.

[210] The EU defines a "tiered price" pharmaceutical as being offered to the poor for either direct manufacturing cost plus no more than 15% or at less than 25% of the OECD weighted average ex-factory price. Council Regulation 953/2003 to avoid trade diversion into the European Union of certain key medicines, art. 7, 2003 O.J. (L135/6) art. 3(a). At these levels of differential pricing, arbitrage is clearly a concern. At present, the EU Council Regulation only applies to exports to 76 listed developing and least-developed countries and to "HIV/AIDS, malaria, tuberculosis and related opportunistic diseases," a limitation which should be amended following Cancun.

[211] Calculated from the data immediately above, assuming that a year's supply weighs about a kilogram.

[212] Or smugglers, depending upon your perspective. The domestic practice is frequent within the United States, even with less significant price incentives to arbitrage. Jackie Judd, Senior Fellow with the Kaiser Family Foundation Speaks with Gilbert M. Gaul and Mary Pat Flaherty, Washington Post Staff Writers on

wealthy countries where they will fetch higher prices. Since the great majority of the world's AIDS patients are in poorer countries, if only a small percentage choose arbitrage, significant volumes of ARVs could flow into OECD markets.[213] Empirical evidence to date does not indicate a sizable arbitrage market in ARVs from poor countries into the OECD.[214]

Pharmaceutical companies stand to lose much from international arbitrage. Combivir™ is GlaxoSmithKline's best selling patented drug, and the company holds a 45% global market share in HIV/AIDS drugs, generating $2.3 billion in global revenue in 2002.[215] Pharmaceutical research companies rely on patent rents to support innovation. If actions to improve financial access to patented drugs result in arbitrage and globally sub-optimal patent rents, then the research enterprise is threatened and prospective quality will have been sacrificed in the name of present access.

B. The Proposed 'Health and Human Rights' Exception to Global IP Laws

The AIDS crisis has fueled claims for a 'health and human rights'[216] exception to global IP laws, permitting the expropriation of drug patents in the face of vast human suffering, akin to a starving child taking a loaf of bread. Many world religions require charity in these circumstances. Jesus expected His disciples to treat the poor fairly,[217] as did King

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a Five-Day Special Report Called "Pharmaceutical Roulette," that Focuses on Prescription Drug Safety Issues in the United States, (Kaiser Family Foundation transcript, Oct. 24, 2003) *available at* www.kff.org (describing significant arbitrage diversion within the US market taking advantage of relatively modest price differentials).

[213] The United States is a likely target market. The EU may not be vulnerable to diversion because most of its citizens are covered by a third party prescription drug benefit, and are not price sensitive. DG Trade, *supra* note 7, at §3.3. This conclusion might be true for ultimate consumers, but perhaps European intermediaries will find arbitrage earnings from this trade.

[214] In October 2002, 6000 packages of HIV/AIDS medicines were found to have been diverted from West Africa to The Netherlands. Graham Dukes, United Nations Millennium Project, Interim Report of Task Force 5 Working Group on Access to Essential Medicines 50, n.1 (Feb. 1, 2004). As of 2002, both the European Commission and the pharmaceutical companies acknowledged that pharmaceutical arbitrage from poor countries into the OECD was "still largely theoretical." DG Trade, *supra* note 7, at §3.3. By comparison, legal pharmaceutical arbitrage within the EU is a thriving business. Peter West & James Mahon, Benefits to Payers and Patients from Parallel Trade (York Health Economics Consortium Working Paper, May 2003) (estimating direct savings of € 631 million in 2002 from legal pharmaceutical arbitrage (parallel trade) within the EU).

[215] Gautam Naik, *Glaxo's HIV Drugs Come Under Pressure: Competition, Calls for Price Cuts Weakens Company's Dominance of Maturing Market*, Wall St. J., Sept. 22, 2003, at B3.

[216] *See generally* any volume of Health and Human Rights: An International Journal, published by the Francois-Xavier Bagnoud Center for Health and Human Rights at Harvard University.

[217] *Luke* 12:33 ("Sell your possessions and give to the poor. Provide purses for yourselves that will not wear out, a treasure in heaven that will not be exhausted, where no thief comes near and no moth destroys") (NIV).

Solomon and the Prophet Isaiah.[218] Proponents also ground their claims in humanitarian traditions and various UN instruments and treaties.[219]

The health and human rights approach suffers from illimitability. While the current debate is largely about AIDS, the health and human rights community will not be limited only to AIDS advocacy.[220] If a health and human rights exception to IP law is established for AIDS, then it may prove impossible to resist extensions to tuberculosis, malaria, cancer, or indeed any condition. The TRIPS Agreement limited the "public health" exception to "measures necessary to protect public health…provided that such measures are consistent with this Agreement."[221] The Doha Declaration interpreting TRIPS covers "public health problems afflicting many developing and least-developed countries, especially those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics."[222] The change was not accidental. The United States argued against expansion, but ultimately conceded the point under pressure.[223] The Cancun Provisional Waiver[224] and the pending Canadian compulsory licensure legislation[225] also are not limited to AIDS, malaria and tuberculosis. Advocates will encourage expansion to cover

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[218] *See, e.g., Proverbs* 28:27 ("He who gives to the poor will lack nothing, but he who closes his eyes to them receives many curses") (NIV); *Isaiah* 11:4 ("but with righteousness he will judge the needy, with justice he will give decisions for the poor of the earth. He will strike the earth with the rod of his mouth; with the breath of his lips he will slay the wicked") (NIV).

[219] *See, e.g.,* U.N. Charter, art. 55 ("the United Nations shall promote: … solutions of international economic, social, health, and related problems"); International Covenant on Economic, Social and Cultural Rights, art. 12, ¶ 1 ("the right of everyone to the enjoyment of the highest attainable standard of physical and mental health").

[220] *See, e.g.,* Jonathan M. Mann et al., eds., Health and Human Rights: A Reader (1999). Nor will it remain limited to AIDS in sub-Saharan Africa, a limit found in many access programs sponsored by pharmaceutical research companies. MSF, Untangling the Web, *supra* note , at table 2.

[221] TRIPS Agreement, *supra* note 2, at arts. 8.1, 27.2.

[222] Doha Declaration, *supra* note 5, at ¶ 1.

[223] During the negotiations leading up to the Doha Declaration of June 2001, PhRMA, the United States, Japan, Switzerland, Australia and Canada argued for limiting the Declaration to "public health crises such as HIV/AIDS and other pandemics." 't Hoen, *TRIPS*, *supra* note 186, at 38-41. The text proposed by developing countries simply stated: "Nothing in the TRIPS Agreement shall prevent Members from taking measures to protect public health." Id. at 39. The final compromise text was closer to the developing countries position. Id. at 40. Essential medicine advocates have declared victory over this ambiguous text. Correa, *Implications of Doha, supra* note 3, at 5.

[224] Two weeks before the September 2003 Cancun meeting of the WTO, a provisional waiver of TRIPS was agreed to by the Members, permitting cross-border shipments of drugs produced under the Doha Declaration. Cancun Provisional Waiver, *supra* note 6; EU Strongly Welcomes WTO Deal On Generic Medicines, IP/03/1189 (Sept. 1, 2003) [hereinafter EU, Cancun] (The EU uses the phrase "Perez Motta text" to describe the Cancun Provisional Waiver). Under the Cancun Provisional Waiver, developing and least-developed WTO Members may import pharmaceuticals produced under compulsory license if the importing country lacks the relevant pharmaceutical production capacity. While the Cancun Provisional Waiver contains no limitation to AIDS, tuberculosis or malaria, its definition of 'pharmaceutical product' refers back to paragraph 1 of the Doha Declaration. Cancun Provisional Waiver, *supra* note 6, at ¶ 1(a).

[225] Steven Chase, *Chretien sets sights on drug legislation for legacy*, Globe and Mail, Nov. 5, 2003 *available at* www.theglobeandmail.com ("Senior officials vow that the bill will not restrict diseases treated").

all of the ailments of the poor.[226] The near-poor will be next in line, followed by the middle class.[227] Each step shrinks the market segments which pay patent rents. At some point, patent rents may become sub-optimal.

It may also prove impossible to limit the exception to health care. While the TRIPS exception relates to public health, the human rights community does not rely upon TRIPS as its foundational text. If human rights are violated by human suffering, claims may be asserted against the wealth of the OECD to alleviate global poverty. The exception is also not greatly limited by restricting it to 'opportunity goods' such as such as health, education, shelter and nutrition. The cost to fulfill these items alone would swallow the rule of private property. While the Bible requires charity and hospitality, it also supports private property: the Eighth Commandment states: "You shall not steal" and the Tenth Commandment promotes respect for private property.[228]

None of this should be taken as an indictment of the health and human rights movement. Their achievements are impressive: the Doha Declaration, the Cancun Provisional Waiver, the Global Fund, NGO provision of health care to millions, a $15 billion commitment from President Bush, and many others. The movement has focused world attention and resources on pressing global health problems. But dogmatic appeals to 'rights' -- whether human or IP – should not be taken too seriously. The language of rights takes the form of absolutes, but the task at hand is to balance the competing needs of access (human rights) with innovation (IP rights).

C. Compulsory Licensure and Differential Pricing

1. TRIPS Enforcement Hinders Delivery of ARVs

The TRIPS Agreement was crafted by OECD companies with strong financial interests in IP.[229] The benefits to the OECD are clear, but TRIPS implementation in developing countries carries severe risks.

The interlocking web of IP and DRA laws significantly hinder distribution of low-cost medicines for the poor.[230] Pharmaceutical research companies did not voluntarily embrace differential pricing of ARVs at a 30:1 ratio. The companies strongly resisted both significant price reductions as well as unlicensed ARV drugs, citing both TRIPS and domestic IP legislation.[231] In response to the high cost of ARVs in low-income

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[226] Correa, *Implications of Doha, supra* note 3, at 5 (Doha 'covers any "public health problem", including those that may be derived from diseases that affect the population in developing as well as developed countries, such as asthma or cancer").

[227] A similar process is underway as the Global Fund expands it programs from the poorest sub-Saharan nations to include middle income countries such as Honduras. WHO, Surmounting Challenges, *supra* note 152, at 25.

[228] *Exodus* 20:15, 17 (NSRV).

[229] Sell, *TRIPS*, *supra* note 149, at 490.

[230] MSF, Untangling the Web, *supra* note 113; WHO, Surmounting Challenges, *supra* note 152.

[231] WHO, Surmounting Challenges, *supra* note 152; 't Hoen, *TRIPS, supra* note 186, at 30-33; Sell, *TRIPS, supra* note 149, at 491-96; Rein, *supra* note 151, at 394-404.

countries, Medecins sans Frontieres and other NGOs violated patents and imported significant quantities of unlicensed ARVs[232] and South Africa passed a compulsory licensing law.[233] South Africa was sued by pharmaceutical research companies for passing this law, and suffered suspension of US bilateral economic assistance as punishment for defending the suit.[234] The US and pharmaceutical research companies relented under great pressure in April 2001.[235]

Brazil has implemented the most effective ARV therapy program outside the OECD. Brazil produced ARVs domestically under compulsory licenses, sparking an outcry from pharmaceutical research companies and the US.[236] In January 2001, the United States requested a WTO panel against Brazil to prevent Brazilian exports of unlicensed AIDS drugs to Africa.[237] Under international pressure, the US withdrew the panel request on June 25, 2001, in the months leading up to the Fourth WTO Ministerial Conference in Doha.[238] The USTR continues to use trade agreements to affect pharmaceutical pricing internationally.[239] As recently as 2002, no person in the developing world had received ARVs through official donor support from any country or multilateral institution.[240]

In a widely-cited study, Attaran and Gillespie-White demonstrated the relative paucity of ARV patents in many sub-Saharan countries.[241] This article has been widely interpreted

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[232] WHO, Surmounting Challenges, *supra* note 152, at 9, 42 (allowing companies set their own differential pricing does not work well in Ukraine for MSF).

[233] Medicines and Related Substances Control Amendment Act No. 90 of 1997 (Republic of South Africa).

[234] Omnibus Consolidated and Emergency Supplemental Appropriations Act, 1999, 112 Stat. 2681-153 (1999) (suspending appropriation of all bilateral economic assistance to South Africa, including AIDS/HIV programs, until steps are taken to repeal section 15(c) of South Africa's Medicines and Related Substances Control Amendment Act No. 90 of 1997). Many commentators have written about the case and the US trade pressure exerted upon South Africa. *See, e.g.,* 't Hoen, *TRIPS, supra* note 186, at 30-31; Lissett Ferreira, *Access to Affordable HIV/AIDS Drugs: The Human Rights Obligations of Multinational Pharmaceutical Corporations*, 71 Fordham L. Rev. 1133, 1155 (2002); Rein, *supra* note 151, at 400-402. Doha paragraph 4 discourages Members from exerting bilateral pressure which hinders the exercise of TRIPS and Doha rights. Correa, *Implications of Doha, supra* note 3, at 12.

[235] Editorial, *South Africa's Moral Victory,* 357 Lancet 1303 (Apr. 28, 2001); John R. Thomas, CRS Report for Congress, HIV/AIDS Drugs, Patents and the TRIPS Agreement: Issues and Options 16 (July 27, 2001) [hereinafter Thomas, CRS Report].

[236] Bermudez, *supra* note 153, at 191-94.

[237] World Trade Organization, Request for the Establishment of a Panel by the United States, Brazil Measures Affecting Patent Protection, WT/DS199/3 (Jan. 9, 2001). Executive Order 13155 had specifically reserved to the United States the right to seek such a panel. Exec. Order No. 13155, 65 Fed. Reg. 30521, 30522 (May 10, 2000) ("this order does not prohibit the United States Government from invoking the dispute settlement procedures of the World Trade Organization to examine whether any such law or policy is consistent with" TRIPS). For an overview of the Brazilian and South African situations by the Congressional Research Service, *see* Thomas, CRS Report, *supra* note 222, at 13-17.

[238] 't Hoen, *TRIPS, supra* note 186, at 38-47; Thomas, CRS Report, *supra* note 222, at 15; Correa, *Implications of Doha, supra* note 3, at 2, n.6.

[239] Becker, *supra* note 178.

[240] *African HIV/AIDS Crisis: Pursuing Both Treatment and Prevention: Hearing Before the Sen. Comm. on Foreign Relations, Subcomm. on African Affairs,* [107th Cong., 1st Sess.] (Feb. 14, 2002) (statement of Jeffrey D. Sachs).

[241] Amir Attaran & Lee Gillespie-White, *Do Patents for Antiretroviral Drugs Constrain Access to AIDS Treatment in Africa?*, 286 J. Am. Medical Assn. 1186 (2001) (after the manuscript was submitted, Merck

to claim that patents do not hinder ARV access in sub-Saharan Africa.[242] This conclusion is not warranted from the data. The sub-Saharan countries identified as lacking patents do not possess the domestic industrial base to manufacture complex pharmaceuticals such as ARVs.[243] Unlicensed ARVs would have to be imported from elsewhere, such as South Africa, Brazil and India. Each of those countries are now covered by applicable ARV patents or TRIPS mailbox applications, and a major focus of TRIPS enforcement has been to shut down exports of unlicensed ARVs from these countries to sub-Saharan Africa. In addition, the mere possibility of a patent filing acts as a deterrent to a generic new drug application in sub-Saharan Africa, since the innovator could undercut the market investment by the generic company. These conditions formed an effective deterrent to ARV commercialization by generic companies, even in the absence of a formal patent filing in every sub-Saharan country. In addition, the legal positions taken by the USTR and pharmaceutical research companies in patent litigation also hindered participation by multilateral and official donors. IP laws clearly delayed utilization of ARVs in sub-Saharan Africa.

2. The Doha Declaration and the Cancun Provisional Waiver

At the Fourth WTO Ministerial Conference in Doha, WTO members agreed to the Doha Declaration as an interpretation of TRIPS.[244] The Doha Declaration allows WTO

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gave a $25,000 grant). Several critical letters to the editor were received for the next volume of the journal. Boelaert, et al., *supra* note 152, at 840-41; Eric Goemaere, et al., *Letter to the Editor*, 287 J. Am. Medical Ass'n 841 (2002); Michael J. Selgelid & Udo Schuklenk, *Letter to the Editor*, 287 J. Am. Medical Ass'n 842 (2002) ("In the world of politics the carefully qualified conclusions of Attaran and Gillespie-White are likely to be misrepresented by pharmaceutical industry lobbyists claiming that "it has been shown that patents do not matter," with the aim of blocking proposed TRIPS agreement amendments that weaken pharmaceutical patent protection in developing countries"). In their reply to these letters, Attaran and Gillespie-White do not make the broad claim that patent laws are no barrier to ARVs in sub-Saharan Africa, but merely suggest that where patents exist, other alternatives can be pursued, such as voluntary licensure or switching to another therapy. Where patents do not exist, they call for unlicensed production, ignoring the industrial infrastructure issue described above. Amir Attaran & Lee Gillespie-White, *In Reply*, 287 J. Am. Medical Ass'n 842-43 (2002). [2003 emory transcript]; *see also* Amir Attaran, *How Do Patents and Economic Policies Affect Access To Essential Medicines In Developing Countries?*, 23 Health Affairs 155 (2004).

[242] Lanjouw, Intellectual Property, *supra* note 47, at 11-12 ("industry uses this fact [the Attaran & Gillespie-White study] to stress that patents in the poorest countries are not impeding access to drugs"); *see, e.g.,* Harvey E. Bale, Jr., *Patents, Patients and Developing Countries: Access, Innovation and the Political Dimensions of Trade Policy*, in The Economics of Essential Medicines 100, 106, n.10 (Brigitte Granville, ed.) (2002). Bale is the head of the international pharmaceutical research company trade association.

[243] Correa, *Implications of Doha, supra* note 3, at Annex 2.

[244] Doha Declaration, *supra* note 5. The legal status of the Doha Declaration is discussed in James Thuo Gathii, *The Legal Status of the Doha Declaration on TRIPS and Public Health Under the Vienna Convention on the Law of Treaties*, 15 Harv. J.L. & Tech. 291 (2002) and by Correa, *Implications of Doha, supra* note 3, at 5. The legal status of the Cancun Provisional Waiver is a joint commitment by WTO Members to abide by its terms in good faith. EU, Cancun, *supra* note 211. Practically speaking, it would be impossible to prevail at DSB on a provision contrary to the Cancun Provisional Waiver. The legal status of both Doha and Cancun are expected to be clarified in a planned 2004 amendment to TRIPS. Cancun Provisional Waiver, *supra* note 6, at ¶ 11; Doha Declaration, *supra* note 5, at ¶ 7. In this process, WTO has demonstrated unexpected legislative flexibility.

Members to take measures to "protect public health and, in particular, to promote access to medicines for all."[245] WTO Members may compel licensure to protect public health, without limitation to AIDS or any particular disease.[246]

The TRIPS Agreement restricts compulsory licenses to domestic use, effectively preventing exports.[247] Since many countries do not have domestic pharmaceutical production capacity, the no-export rule prevents many countries from delivering low-cost ARVs to HIV/AIDS patients.[248] Compulsory licenses are not useful to Malawi absent the opportunity to import from Brazil, India or South Africa. The ensuing debate was energetic, leading up to the Cancun WTO meeting in 2003.

Immediately prior to the Cancun meeting, on August 30, 2003, the US conceded the point. Under the Cancun Provisional Waiver, the WTO now permits exports of compulsory licensed drugs to poor countries.[249] The Cancun Provisional Waiver also established a WTO notification process for cross-border compulsory licenses. The TRIPS Council must be notified, but WTO approval is not required.[250] In May 2004, Canada amended the Canadian Patent Law to permit compulsory licenses for certain drug exports to needy nations.[251] As of June 2004, no WTO Member has notified the TRIPS Council.[252]

3. The Necessity of Compulsory Licensure

Voluntary programs of differential pricing have been problematic. Each pharmaceutical research company creates idiosyncratic policies specifying which countries qualify for differential pricing on any particular drug. Transaction costs are high when essential access discounts are negotiated on a case-by-case basis.[253] Essential access policies vary by the status of the purchaser (NGO, IGO, government, private buyer). Many of these policies are limited to sub-Saharan Africa or specific low-income countries, thereby excluding AIDS crises in Asia, the former Soviet states, Latin America or most of the Caribbean.

Voluntary programs of differential pricing also fail to achieve differential pricing at the marginal cost of production, which is absolutely necessary in low-income countries.

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[245] Doha Declaration, *supra* note 5, at ¶ 4.
[246] Doha Declaration, *supra* note 5, at ¶ 5; 't Hoen, *TRIPS, supra* note 186, at 40-41. US law permits compulsory licenses by the federal government. See *supra* note [156] and text accompanying.
[247] TRIPS Agreement, *supra* note 2, at art. 31(f).
[248] *See* Doha Declaration, *supra* note 5, at ¶ 6.
[249] Cancun Provisional Waiver, *supra* note 6. EU, Cancun, *supra* note 211.
[250] Cancun Provisional Waiver, *supra* note 6, at ¶ 2. Notice must be given to the WTO, but approval is not part of the process. EU, Cancun, *supra* note 211.
[251] The Jean Chretien Pledge to Africa Act, House of Commons, 3rd Sess., 37th Parliament, 52-53 Eliz. II, 2004 (Bill C-9) (received Royal Assent on 14 May 2004). The law created a positive list of drugs eligible for compulsory licensure, a procedural hurdle not required by the WTO. Id. at Schedule 1.
[252] The WTO has established a webpage to announce notifications under Doha and Cancun, http://www.wto.org/english/tratop_e/trips_e/public_health_e.htm. None are posted as of June 10, 2004.
[253] MSF, Untangling the Web, *supra* note 113, at 5.

Voluntary negotiations kept ARV prices unnecessarily high for years and delayed effective treatment for millions of dying people. Sovereign threats of compulsory licenses, public pressure from NGOs, and actual competition from unlicensed generic companies persuaded pharmaceutical research companies and the US to embrace significant ARV differential pricing for poor countries.[254] Compulsory licensure enables ex-factory pricing closer to true marginal manufacturing cost, particularly if the tender process is competitive. Generic competition pierces the pricing veil, accelerates differential pricing towards true marginal production costs, and does not rely on public disclosure of confidential financial information from the companies. Given the endemic opacity of all PhRMA data on costs, perhaps the best way to calculate marginal cost is through compulsory licensure.[255]

Compulsory licenses are difficult to administer under TRIPS. The procedures are time-consuming and expensive. Companies may delay utilization for many months or years, while both sides employ advocates to press their positions. This process is wasteful, particularly when duplicated in multiple countries. But without the credible threat of compulsory licenses, innovators have few reasons to cooperate with differential pricing, particularly for global diseases outside of the media glare of AIDS.

D. Preventing Pharmaceutical Arbitrage into OECD Markets

If non-market patients are to receive needed medications, steps must be taken to support differential pricing and block pharmaceutical arbitrage into OECD markets.[256]

One option is to increase transaction costs for smugglers through monitoring and enforcement action. The Cancun Provisional Waiver requires importing countries to implement reasonable measures to prevent diversion and re-exportation. "Reasonable" measures must be "within their means" and "proportionate to their administrative capacities and the risk of trade diversion."[257] Under Cancun, developing and least developed countries inappropriately bear these costs even if global patent rents are supra-optimal.[258]

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[254] *See* the discussion in Section IV.C.2 *supra.*

[255] PhRMA simply asserts that "there is no guarantee that generic companies will price at marginal cost." Graham Dukes, UN Development Programme, Interim Report of Task Force 5 Working Group on Access to Essential Medicines App. 2, at 27 (Response of the Research-Based Pharmaceutical Industry to the Interim Report of the Task Force on Access to Essential Medicines) (Feb. 1, 2004). Absent the patent monopoly, generic companies in a competitive environment will certainly price much closer to marginal cost than PhRMA companies.

[256] As discussed previously, arbitrage within OECD markets, or between low-income countries, should be permitted so long as these actions are unlikely to lead to sub-optimal patent rents. Likewise, exports of differentially priced drugs into low-income countries should be permitted, even if the source is an OECD country like Canada. The only arbitrage which must be prevented is from low-income countries to OECD countries. *See* Section IV.C.3. *infra.*

[257] Cancun Provisional Waiver, *supra* note 6, at ¶ 4.

[258] If global patent rents are supra-optimal, these costs could be borne by the pharmaceutical research companies without harming innovation. Placing the burden on countries with annual per capita health budgets of $100 or less is exceedingly unfair.

A second option is to control production and distribution. Careful control of vaccines from production to administration has effectively defended differential pricing, although this process is much more difficult with medications taken on a daily basis.[259] Experience with counterfeiting suggests that control over sophisticated manufacturing processes lowers enforcement costs by hindering source proliferation. If so, pharmaceutical research companies should agree to produce the drugs themselves at marginal production cost, or allow parallel importation from reputable manufacturers. Otherwise, other companies must independently develop manufacturing expertise which may then be diverted. The Cancun Provisional Waiver now permits poor countries without domestic pharmaceutical manufacturing capacity to import pharmaceuticals produced under a compulsory license.[260]

A third option is to modify the product to resist substitutability. The pharmaceutical manufacturing process could be altered to create multiple versions of any prescription drug, distinguished by radically different colors, shapes, names, sizes and packaging. Markets must be segmented into commercial and charitable markets, and never the twain shall meet. The Cancun Provisional Waiver addresses this issue: exporting countries must clearly identify the products through labeling or marking and through special coloring or shaping.[261] The EU recently acted to adopt a Council Regulation designed to hinder diversion into the EU market, including alteration of appearance.[262]

Fourth, consumers can be persuaded to resist substitution. Advertising could be directed to commercial market consumers, warning them never to take the red pills with labels in Swahili. This is also an implicit safety warning: those pills may not be as safe. One weakness is that Africans will be told exactly the opposite: the red pills are safe and effective.[263] Other advertising could describe substitution as a moral issue: OECD patients who take pills intended for impoverished Africans are stealing from the poor.[264] Under the EU Council Regulation, all covered pharmaceuticals exported from the EU will bear a special logo identifying the product as destined for the poor.[265]

Fifth, virtual pharmaceutical arbitrage into OECD countries should be banned outright under TRIPS. Virtual pharmaceutical arbitrage occurs when an OECD market uses differential prices for the poor under its national external reference pricing scheme.[266]

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[259] DG Trade, *supra* note 7, at §3.8.
[260] *See* Section V.C.2 *infra.*
[261] Cancun Provisional Waiver, *supra* note 6, at ¶ 2(b).
[262] Council Regulation 953/2003 to avoid trade diversion into the European Union of certain key medicines, art. 7, 2003 O.J. (L135/5) ¶10. While the Council Regulation addresses importation in luggage for personal use, similar to the US personal importation rule, it does not address (but probably covers) internet sales. *Id.* at ¶13, art. 10. Seized product may be used for humanitarian purposes. *Id.* at ¶14.
[263] Vertical product differentiation based on quality is common in some products (regular v. premium gasoline), but is probably untenable in pharmaceuticals.
[264] If the arbitraged drugs were voluntarily sold rather than stolen, then the moral claim weakens.
[265] Council Regulation 953/2003 to avoid trade diversion into the European Union of certain key medicines, art. 7, 2003 O.J. (L135/7). The logo is found in Annex V of the regulation.
[266] *See supra* notes 173-74 and text accompanying in Section IV.C.6.

These strategies are likely to be fully effective, which is why companies are reluctant to voluntarily embrace aggressive differential pricing. A small amount of international arbitrage might be tolerable. The likely OECD consumers of smuggled African AIDS drugs might well be at the margins of the nation's health care system. These patients may not be market participants either, despite their physical location in an OECD nation.[267] So long as commercial markets are not replaced, the practice will not harm innovation. Modest leakage from commercial markets would reduce patent rents, but may or may not harm innovation.

E. Domestic Market Arbitrage and Third-Degree Differential Pricing

The current TRIPS approach is tied to state sovereignty, creating differential pricing along national political boundaries. Full TRIPS implementation is now delayed until 2005 for many countries, and until 2016 for the 30 WTO Members which are classified as least-developed.[268] This state-centric system is not surprising, given that only states are Members of the WTO, but system suffers from both over-inclusion and under-inclusion.

Over-inclusion occurs when an entire nation is granted an exception or extension under TRIPS, even though some people within the poor countries can afford to pay market prices for the drugs. Even in the poorest countries, an elite cadre of individuals control enough wealth to afford these drugs. In countries such as India, Brazil, Chile, Mexico, South Africa and China, these markets are small but growing.[269] Providing low-cost AIDS drugs to South Africa might make it more difficult to charge full price to wealthy or middle class South Africans, absent effective segmentation of the markets. The elites in non-OECD countries are in actuality part of the "OECD market," and should be expected to participate in the market on normal commercial terms.

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[267] For this reason, the confiscation of 6,000 packages of 'African' AIDS medications in The Netherlands in October 2002 might not represent a major threat to innovation. Dukes, *supra* note 122, at 50, n.1.

[268] Doha Declaration, *supra* note 5, at ¶ 7. This delay applies only to pharmaceutical products.

[269] For example, in South Africa, the NGO and public sector price for a triple therapy regime (ZDV/3TC+NVP) was US$400 per person year while the private sector price in South Africa was US$2007. WHO, Surmounting Challenges, *supra* note 152, at 37. Pharmaceutical companies may currently prefer to keep the small full-priced elite market in developing nations rather than risk arbitrage. Oxfam, *supra* note 122, at 93 (drug companies target elite households in Argentina, Brazil, India and China); W. Duncan Reekie, *The Development Trilemma and the South African Response*, in Brigitte Granville, ed., The Economics of Essential Medicines 161, 167 (2002) (The top 20% of South Africans enjoy a per capita GNP of $27,699, comparable to OECD levels, and are therefore a significant market for drug companies); WHO-WTO, *Differential Pricing and the Financing of Essential Drugs,* in Brigitte Granville, ed., The Economics of Essential Medicines 209, 213, 220 (2002) (recognizing elite drug markets in developing nations); Scherer & Watal, *Post-TRIPS Options, supra* note 160; Patricia Danzon & Michael Furukawa, Prices and Availability of Pharmaceuticals: Evidence from Nine Countries exh. 8 (undated presentation, on file with author) *available at* http://hc.wharton.upenn.edu/danzon/index.htm (prices normalized by national income in Chile and Mexico are 528% and 529% of the US prices; I interpret this data to mean that drug purchasers in Chile and Mexico must have personal incomes far in excess of the national average). In their public filings with the US Securities and Exchange Commission, PhRMA companies acknowledge the growing middle class markets in the developing world. Merck & Co, Inc., Form 10-k (filed with the SEC on Mar. 10, 2004) at 14.

Under-inclusion occurs when a country does not qualify for TRIPS special treatment as a least-developed country, despite the presence of a desperately needy population who cannot afford patented prescriptions. The state-centric system lays responsibility for these low-income patients on the middle-income countries in which they reside.

This imperfect condition may be called *third-degree differential pricing*. Recall that first-degree price discrimination maximizes gross revenue, but high transaction costs require the aggregation of individual buyers into larger market segments.[270] In a similar fashion, TRIPS aggregates customers into national markets, reflecting both transaction costs and the political realities of sovereignty. These market segments are defined by state political borders rather than actual health needs or ability to afford medicines. Political segmentation of markets creates over- and under-inclusion, to the detriment of the public health. Absent transaction costs, *first-degree differential pricing* would extend aggressive differential pricing to the poor of every country, regardless of location. First-degree differential pricing maximizes access, but transaction costs intrude once again, as will the opportunities for domestic arbitrage.

Some form of third-degree differential pricing is the only realistic option, but segmenting the markets on national boundaries is not required. If domestic arbitrage were blocked between the commercial and charitable sectors, then pharmaceutical research companies could retain the elites market in low- and middle-income countries. Furthermore, if global patent rents are supra-optimal, pharmaceutical research companies could bear the loss of some elite markets without harming innovation, allowing a shift down the continuum towards first-degree differential pricing on sub-national levels. Many OECD countries practice differential pricing on the sub-national level.[271]

F. Implications for Ongoing Modifications to TRIPS

The TRIPS Agreement is scheduled to be amended to incorporate both the Doha Declaration and Cancun Provisional Waiver.[272] As part of that process, TRIPS can be modified in three ways to improve drug access while strengthening innovation: (1) Expand the Doha consensus to all global diseases, so long as actual and virtual arbitrage from target markets into OECD markets are restricted; (2) Streamline the global process for differential pricing and compulsory licensure of patented pharmaceuticals, taking unnecessary costs out of the system, and enhancing the effectiveness of the enforcement mechanisms through global coordination; and (3) Expand the list of countries eligible to participate, so long as serious efforts to block domestic arbitrage are undertaken.

1. Doha and Cancun Did Not Harm Global Pharmaceutical Innovation

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[270] *See* Section II.A *supra.*

[271] In the US, drug prices vary significantly by payor class, such as Medicare, Medicaid, Veterans' Affairs, private insurers, FEHBP and private payors. Price discrimination causes uncovered individuals to frequently pay the highest prices for pharmaceuticals. CBO, Increased Competition, *supra* note 28, at xi.

[272] The WTO is expected to amend TRIPS to reflect the Doha Declaration and the Cancun Provisional Waiver. EU, Cancun, *supra* note 211; Cancun Provisional Waiver, *supra* note 6, at ¶ 11.

One misapprehension about Doha and Cancun is that AIDS activists and developing countries won at the expense of global innovation. In fact, the compromise is fully supportive of global pharmaceutical innovation: differential pricing for the poor is provided together with restrictions on pharmaceutical arbitrage into the OECD. Differential pricing may be safely expanded to all global diseases without risk to innovation, so long as arbitrage is blocked. [273] Differential pricing may also become more aggressive, moving towards marginal production costs.

Similarly, the decision by the Global Fund to procure drugs as the lowest possible price, including generics, is warranted.[274] By contrast, the US Emergency Plan for AIDS Relief calls for only 6.3% of the $15 billion to be placed with the Global Fund, with the remainder devoted to bilateral US efforts,[275] which may restrict procurement to higher-priced medications.[276] In conditions of supra-optimality, this shift is an unnecessary subsidy of pharmaceutical research companies, diverting scarce donor funds from AIDS projects.

2. A Revised TRIPS Compulsory License Could Improve Access to Essential Medicines While Protecting Against Inappropriate Arbitrage

The TRIPS Council could streamline essential access procurement by joining with WHO to create a centralized alternative to ad hoc negotiations and litigation: a global non-exclusive compulsory license process for generic production of essential access medications.

Essential features of this TRIPS/WHO license would include: (1) A uniform process for creating and amending a list of target populations[277] and a list of essential access drugs;[278] (2) These drugs could be deemed to comply with the patent and DRA laws of the relevant countries, a form of 'reference approval;'[279] and (3) The compulsory license royalty will

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[273] *See* Section IV.C.1 *supra*.

[274] The Global Fund for AIDS, Tuberculosis and Malaria, Procurement and Supply Management, a Presentation of Preliminary Guidelines (May 13, 2003) (*available at* http://www.theglobalfund.org).

[275] The President's Emergency Plan for AIDS Relief: U.S. Five-Year Global HIV/AIDS Strategy 16 (Feb. 23, 2004).

[276] Sarah Lueck & Michael M. Phillips, *U.S. Awards Grants in AIDS Battle: Disbursement is First Part of a $10 Billion Pledge; Generics Issue is Unresolved*, Wall St. J., Feb. 24, 2004, at D 5 (raising unresolved questions about whether the Office of the US Global AIDS Coordinator will procure generic AIDS drugs at the lowest possible price).

[277] The term 'populations' is used in lieu of 'countries,' recognizing the inclusion issues raised in Section V.E *supra*.

[278] While the movement uses the term 'essential medicines,' this list should include all safe and effective patented drugs for global disease conditions. The WHO Essential Medicines List is much more restrictive, and until recently did not include most patented medications, under the assumption that patented medicines would be unavailable to the poor.

[279] In 2001, the WHO began the Pre-Qualification Project, which is a first step in this direction. *See* http://mednet3.who.int/prequal/default.shtml. A reference approval system requires two additional steps. First, drug approval would be referenced against approval in OECD countries. For example, if a drug was approved by either the US FDA or the EU, then it would automatically meet safety and efficacy standards in the target country. Second, WHO Pre-Qualification (or a similar process) would be deemed to satisfy other domestic DRA requirements such as good manufacturing practices. Reference approval reduces

vary by the drug and target population, and may be zero for low-income populations or higher amounts for middle-income populations.

Finally, TRIPS must intensify measures to prevent inappropriate arbitrage, such as globally uniform marks and pedigrees for essential access medications, WTO Member undertakings to establish civil and criminal penalties for essential access diversion, and OECD measures to hinder importation.

3. Expand the List of Countries Eligible for Differential Pricing

As of January 1, 2005, concessions under TRIPS will be largely limited to the 30 poorest members of the WTO, excluding countries such as Mexico, India, China and Brazil. Differential pricing should be extended to target populations in a larger group of countries. If patent rents are supra-optimal, loss of some elite markets will not harm innovation. Even if patent rents are sub-optimal, additional countries can receive differential pricing if they undertake serious measures to segment and protect the local elite OECD market. As the AIDS epidemic widens to Eastern Europe and Central Asia, access must be expanded in regions beyond sub-Saharan Africa.[280]

VI. Pharmaceutical Arbitrage from Canada

Pharmaceutical arbitrage is not just a concern of low- and middle-income countries; millions of US residents are importing cheaper patented drugs from Canada and elsewhere, the 'Boston Tea Party of the 21st Century.'[281]

A. The Opportunity for Arbitrage

Patented drug prices in the United States are generally the highest in the world.[282] Most other OECD countries have regulatory structures which significantly limit prices for

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duplication and lowers non-patent barriers to essential medicines. The US has opposed expansion of the WHO prequalification process. In the 2004 World Health Assembly, the US pushed to remove the word "strengthening" from the WHO HIV/AIDS Resolution. Cmp. World Health Organization, A57/A/Conf.Paper No. 3 Rev. 1, 20 May 2004 with Rev.2 (May 21, 2004). The word was retained in the final document. WHO, Fifty-Seventh World Health Assembly, Scaling up Treatment and Care Within a Coordinated and Comprehensive Response to HIV/AIDS, WHA57.14 (May 22, 2004) at 3(3). The US also opposed reference marketing approvals in the Central American Free Trade Agreement. [cite]

[280] Gideon Long, *Africa Casts Long Shadow over EU AIDS*, Reuters Health Information, Feb. 23, 2004.

[281] Senator Joe Lieberman, Democratic Presidential Debate in Goffstown, New Hampshire, Jan. 22, 2004, *available at* http://www.washingtonpost.com/wp-dyn/articles/A39875-2004Jan22.html, *quoted in* Donald L. Bartlett & James B. Steele, *Why We Pay So Much for Drugs,* Time, Feb. 2, 2004, at 46

[282] US patented prescription drug prices are the highest of any major market, with the possible exception of Japan. Danzon & Furukawa, *supra* note 253, at exh. 3. Generic drugs, unprotected by patents or exclusive marketing periods, are generally priced competitively in the US. Comparisons of international drug prices should not conflate the categories. Danzon and Furukawa fault other studies for excluding generics since they represent significant volumes in the OECD. Id., at 4. However, generics must be excluded when calculating patent rents or the potential for arbitrage in patented drugs. Canadian prices are 64% of US prices for patented drugs, and somewhat higher for generics, yielding a net differential of 6%. Id., at exh. 4. *See also* Letter from William K. Hubbard, Associate Commissioner for Policy & Planning, FDA, to

patented pharmaceuticals.[283] Canada's Patented Medicine Prices Review Board[284] helps to keep Canadian prices significantly lower than US prices for patented drugs.[285] This significant differential pricing invites consumer arbitrage.

The first phase of the Canadian-US arbitrage involved individuals purchasing drugs while traveling in Canada for other reasons, such as vacation or business. This arbitrage was usually limited to people who got sick while in Canada, or who unexpectedly exhausted their US prescriptions while traveling. Marginal transaction costs were negligible for those persons already in Canada.

The second phase was more strategic on the part of consumers. Some US consumers noticed the price differentials when filling prescriptions in Canada. People living close to the border could make short intentional trips to fill lower-cost prescriptions, with a transaction cost of a few dollars and a modest amount of time. Bus trips were subsequently organized for people living at greater distances, specifically to stock up on patented medications. Politicians – particularly those from states near Canada - began to sponsor the trips. The transaction costs for these trips were greater – several hundred dollars and significant time – but for some consumers, the cost savings were greater still. As consumers became more accustomed to mail order pharmacies, repeat customers could avoid the transaction costs of another trip and re-order by mail from Canada. Consumer arbitrage began to erode differential pricing between US and Canadian drug prices.

Ram Kamath & Scott McKibbon, Special Advocates for Prescription Drugs, State of Illinois (Nov. 6, 2003) (on file with author) (generics generally cheaper in the US compared to Canada). Thus the potential for arbitrage lies in the 36% differential in patented medications, not the 6% overall figure.

[283] Rothnie, *supra* note 43, at 491 ffg. (general, but dated, discussion of EU pharmaceutical price controls); s*ee also* Danzon, et al., *supra* note 165 (pharmaceutical companies delay launch of new drugs in EU countries with strict price controls to reduce risk of parallel trade).

[284] Since 1988, Canada regulates patented drug prices through the Patented Medicine Prices Review Board, a quasi-judicial board with can bring proceedings against pharmaceutical research companies which charge excessively high prices. Barrados, *supra* note 86, at ¶17.6 – 17.17; Dr. Robert G. Elgie, Canada's Patented Medicine Prices Review Board: New Approaches (Drug Industry Ass'n Washington Conference on Pharmaceutical Pricing and Reimbursement: What New Variables are at Work? 3-4 (Patented Medicine Prices Review Board, Ap. 16, 1999) *available at* http://www.pmprb-cepmb.gc.ca. The Board has effectively constrained patented drug prices in Canada. Barrados, *supra* note 86, at ¶17.25. Since the creation of the Board, patented pharmaceutical prices in Canada have increased only 1% per year on average. Elgie, *supra,* at 6. Nevertheless, Canada's system is not strictly a price control or rate setting system, but a soft reference price system with a quasi-judicial process. Barrados, *supra* note 86, at ¶17.50 – 17.56; Elgie, *supra*, at 6.

[285] Many surveys have documented the price differential between US and Canadian patented pharmaceuticals. *See, e.g.,* Ram Kamath & Scott McKibbin, Office of Special Advocate for Prescription Drugs, State of Illinois, Report on Feasibility of Employees and Retirees Safely and Effectively Purchasing Prescription Drugs from Canadian Pharmacies 79 (2003) (39% savings on the drugs that Illinois purchases that could be safely imported from Canada); Danzon & Furukawa, *supra* note 253, at exh. 4 (patented drugs are 36% cheaper in Canada compared with US); *Savings Immense on Canadian Drugs*, Wash. Times, Nov. 5, 2003 *available at* www.washtimes.com/national/20031105-112757-6536r.htm (33% to 80% cheaper for the 10 most popular drugs). If Canadian patented pharmaceuticals continue on their 1% price rise trajectory, and US drug prices continue to inflate at a greater rate, then the US – Canadian price differential will increase for the indefinite future. US retail prescription drug prices are expected to increase at 12.9% in 2004 and 12.4% in 2005. Heffler, et al., *supra* note 130, at exh. 2.

These early forms of arbitrage were limited in several ways. Only drugs for outpatient non-emergency use could be easily substituted. The initial buyers were Americans who exhausted their personal drug supplies while traveling in Canada. The high transaction costs of travel to Canada limited the scope and potential expansion of this market. Information costs were also significant. Canadian pharmacies did not significantly advertise in the US during this phase of the market. Knowledge of the arbitrage opportunity was largely gained by word of mouth or opportune discovery.

1. The Internet Enables More Extensive Arbitrage

The internet dramatically altered the potential for pharmaceutical arbitrage. The transaction cost of importing a prescription from Canada dropped to a small fraction of the arbitrage savings.[286] Many Canadian websites began to compete for the American consumer's attention. These factors multiplied the possible arbitrage market. The potential number of buyers for cross-border arbitrage jumped from several million Americans living near the Canadian border to the entire wired population of the United States. In last several years, the potential number of buyers expanded again, as US-based companies began to facilitate internet ordering of pharmaceuticals for unwired consumers, particularly the elderly. Health insurers and some government officials began to encourage consumers to acquire cheaper medicines from Canada. The media devoted increasing attention to the phenomenon from 1999, raising awareness amongst consumers that arbitrage was an option. A large and growing portion of the most valuable market for patented pharmaceutical medications is now only a click away from arbitrage.

If this process continues unchallenged, one would expect institutions such as hospitals, nursing homes, and retail pharmacies to begin to source from Canada. Payors such as health plans[287] and governments[288] are now following suit. The State of Illinois recently recommended importing patented drugs from Canada for its employees and retirees. The State of Illinois estimates that $250 million of its prescription drug costs could be sourced from Canada,[289] with potential savings of $90.7 million per year.[290] Several other states are exploring similar programs.[291] These state efforts are being blocked by the FDA.

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[286] For a patient with annual prescription costs of $2000, a reasonable amount of search costs can be justified to save 30%.

[287] United States-based PBMs are paying claims today from Canadian pharmacies, supporting the patient's decision to import, Kamath & McKibbin, *supra* note 264, at 13, as are some large health plans such as UnitedHealth. Thomas M. Burton, *The FDA Begins Cracking Down on Cheaper Drugs from Canada*, Wall St. J., Mar. 12, 2003, at A1.

[288] The State of Illinois is aggressively pursuing a plan to import patented medications from Canada beginning April 1, 2004, if FDA approval is given. Kamath & McKibbin, *supra* note 264, at 3, 30.

[289] Kamath & McKibbin, *supra* note 264, at 79-81.

[290] Kamath & McKibbin, *supra* note 264, at 19 (cost savings assumes all employees and retirees will participate).

[291] *See, e.g.,* Katherine M. Skiba, *Doyle Makes Case for Buying Cheaper Drugs from Canada,* Milwaukee Sentinal-Journal, Feb. 24, 2004; Fred Frommer, *Pawlenty Tries to Win FDA over on Drug Plan*, Minneapolis Star Tribune, Jan. 16, 2004 (Minnesota Governor's attempt to win FDA approval for drug importation plan); Tony Leys, *Vilsack Offers Plan on Canadian Drugs*, DesMoines Register, Jan. 22, 2004 (Iowa's plan).

The current level of arbitrage is already significant in the Canadian market. In 2004, the US retail prescription drug market is an estimated $207.9 billion.[292] In October 2003, an FDA official estimated that 3 million US prescriptions per year were being filled from Canada,[293] yielding an estimated arbitrage market size of $600 to 700 million per year in 2003.[294] The State of Illinois program alone could add $250 million to this market, demonstrating the potential for growth. Canadian expenditures on prescribed pharmaceuticals in 2002 were CAN$14.573 billion,[295] thus the arbitrage market is already a significant part of the overall Canadian market.

Unlike ordinarily fleeting opportunities for financial arbitrage, this market is not self-correcting. Canadian prices will not increase much, given government regulation;[296] normal US prices will not fall unless the pharmaceutical research companies agree to reduce their monopoly price. If the supply of patented drugs in Canada remains sufficient,[297] a permanent arbitrage opportunity results and will persist for as long as the patent remains in force. With negligible transaction and information costs, a fungible product in abundant supply, and non-responsive pricing, one would expect a large portion

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[292] Heffler, *supra* note 130, at exh. 1. This number includes only retail sales of prescription drugs, excluding purchases of prescription drugs by institutions such as hospitals and nursing homes. The all-inclusive number for 2004 is closer to $250 billion. Alan Sager & Deborah Socolar, Do Drug Makers Lose Money on Canadian Imports? 4, n. 25 (Boston University Health Reform Program, Data Brief No. 6, April 15, 2004).

[293] Transcript of motion for preliminary injunction at 127-28, United States v. Rx Depot, Inc., No. 03-CV-0616-EA (M) (N.D. Ok. Oct. 8-9, 2003) (examination of Thomas McGinnis, Director of Pharmacy Affairs, FDA) (on file with author) [hereinafter Rx Depot Transcript].

[294] While the average size of US – Canadian prescriptions are unknown, data from the State of Illinois describes consumer co-pays of at least $40 per prescription, Kamath & McKibbin, *supra* note 264, at 5, implying a retail price of $200 at a 20% co-pay. One internet facilitator's data indicated an average Canadian prescription price of $220. Private interview by author, October 2003. Recent Canadian estimates suggest a market of $700 to $800 million per year. Tamsin Carlisle, *Some Online Pharmacies Aren't Filling Big Orders Due to Fears of Shortages,* Wall St. J., Dec. 26, 2003, at A9; Tony Pugh, *Low-Cost Drug Sales to U.S. Should Stop, Canadian Group Says*, Philadelphia Inquirer, Nov. 16, 2003, *available at* www.philly.com. Other recent studies have reached similar estimates for the size of the Canadian arbitrage market. Sanger & Socolar, *supra* note 280, at 4 ($695 million in 2003, based on IMS data). The largest US retail drug store chain, CVS, estimates that US patients spend $3 billion a year outside the USA. Pharma Marketletter (May 17, 2004). By comparison, the domestic US prescription mail order market was $20.7 billion in 2001. NIHCM Foundation, Prescription Drug Expenditures, *supra* note 177, at 9.

[295] Canadian Institute for Health Information, *supra* note 24, at 66. Precise comparisons with US pharmaceutical sales are difficult. The Canadian figures exclude sales to non-Canadians (including cross-border internet sales) but include institutional sales (which are excluded from the comparable US statistics).

[296] Pharmaceutical research companies recently announced small price increases permitted by the Patented Medicine Prices Review Board. Bernard Simon, *Curtailing Medicines From Canada,* N.Y. Times Nov. 11, 2003. These price increases were targeted against drugs in the US arbitrage market. Pharmaceutical research companies are also attempting to limit the supply of drugs provided to Canada to hinder cross-border arbitrage, encouraging shortages and retail price increases. *Id.* Both actions are designed to hinder arbitrage.

[297] *But see* Section VI.B.2.a *infra.*

of the available US market to source from Canada, limited only by the capacity of the Canadian market to handle the volume.[298]

Canadian arbitrage may destroy the differential pricing system which kept US drug prices the highest in the world. Erosion of differential pricing will shift consumer surplus from producers to consumers. American consumers will save many billions of dollars on pharmaceuticals, greatly improving financial access. The other side of the coin is that pharmaceutical research companies will lose the lion's share of their worldwide profits.[299] One unasked question is whether this process will result in sub-optimal patent rents. Supporters of pharmaceutical companies simply assume that drug innovation will be hindered. So long as patent rents remain supra-optimal, Canadian arbitrage improves consumer welfare without harming innovation.

2. Regulatory Arbitrage

A process similar to arbitrage also occurs between regulatory systems. Within the United States, if one particular state imposes draconian regulations upon businesses, the business owners may vote with their feet by relocating to a more attractive regulatory environment. If sufficiently important firms relocate, or credibly threaten to do so, then the state may reconsider its stance and ameliorate the harsh regulations.[300]

A variation of this process is at work in Canadian arbitrage. In the United States, pharmaceutical companies have been largely successful in blocking the adoption of price controls for its products.[301] Other nations, such as Canada, have imposed more restrictive regulatory measures to reduce patent rents.[302] One perspective on this cross-border arbitrage is that some Americans have imported Canada's pricing regulatory system into

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[298] A recent CBO issue brief suggests that the net effect on US prices from Canadian arbitrage will be small. CBO, Would Prescription Drug Importation Reduce U.S. Drug Spending? (Apr. 29, 2004). The CBO assumed that arbitrage supplies would be successfully interdicted by PhRMA companies, capping the arbitrage at 10 to 15% of the US market, and assumed no competitive price reductions in the US. Id. at 4-6. Even under the CBO's pessimistic assumptions, the 10 year savings to US consumers will be $40 billion. Id. at 8. Put another way, PhRMA's reduced profits from legalizing OECD arbitrage will be $40 billion over 10 years.

[299] Alan Sager and Deborah Socolar dispute this conclusion, claiming that Canadian arbitrage need not reduce the profits of pharmaceutical research companies, but their conclusion requires that a high percentage of arbitrage purchases actually represent new aggregate demand. Sager & Socolar, *supra* note 280, at 1 ("We find that if new prescriptions' share of imports is 44.53 percent or more, importing actually increases drug makers' profit.) The question will turn on whether pharmaceutical demand is relatively inelastic. *Id.* At 11-13.

[300] The classic work is Charles Tiebout, *A Pure Theory of Local Expenditures,* 64 J. Pol. Econ. 416 (1956).

[301] The industry strongly oppose price controls. Sidney Taurel, *Hands Off My Industry*, Wall St. J., Nov. 3, 2003, at A14 (Taurel is President, Chairman and CEO of Eli Lilly).

[302] Many discussions of Canada's patented pharmaceutical pricing system wrongly assume it includes mandatory price controls. Canada's Patented Medication Prices Review Board uses a soft reference prices and quasi-judicial processes to regulate the ex-factory prices within Canada. The Board also encourages R&D at a minimum level of 10% of revenues, and grants special pricing consideration to breakthrough drugs. Barrados, *supra* note 86, at ch. 17; Elgie, *supra* note 263, at 3-4. Thus, Canada's system is one attempt to optimize patent rents, striking a balance between cost, quality and access, based upon imperfect data.

the US for outpatient non-emergency pharmaceuticals.[303] Regulatory arbitrage is at work between the US and Canada.

Regulatory arbitrage encourages domestic political reaction. Constituents' demands for pharmaceutical arbitrage has led the Congress to pass the MEDS Act, which legalizes the process once the Secretary of Health and Human Services certifies its safety and cost savings.[304] The certification proved to be the Achilles heel, since HHS has refused to issue the certification.[305] The Medicare Prescription Drug and Modernization Act of 2003, as passed by the House of Representatives, permitted importation from Canada without requiring the Secretary's approval.[306] The Pharmaceutical Market Access Act of 2003, also passed by the House, permitted imports from 25 countries with effective DRAs.[307] The Senate version of the bill reinstated the certification requirement, effectively gutting Canadian importation under the Bush Administration.[308] Most observers would not expect a majority of the US Congress to enact Canada's price regulatory system for the United States; nevertheless, existing federal law (if certified by HHS) would achieve a similar result, in response to consumer exploitation of arbitrage opportunities.[309]

Another example of regulatory arbitrage involves the efforts of US psychologists to obtain prescribing authority, currently denied to them under US law. Some US psychologists direct their patients to Canadian pharmacies, which accept prescriptions written by US psychologists.[310] This practice will provide empirical evidence of the medical efficacy of prescriptions by US psychologists, a form of self-directed research.

In both cases, regulatory arbitrage focuses debate on the comparative advantages of alternative systems of regulation. This process should be encouraged, as it promotes

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[303] The American Enterprise Institute identifies this as a major weakness of proposals to permit re-importation from Canada. John E. Calfee, *The High Price of Cheap Drugs*, (Jul. 14, 2003) *available at* www.aei.org.

[304] Medicine Equity and Drug Safety Act of 2000, Pub. L. 106-387, 114 Stat. 1549A-35.

[305] Sarah Lueck, *Senate Supports Wider Importing of Canada Drugs*, Wall St. J., June 23, 2003, at A10.

[306] Medicare Prescription Drug and Modernization Act of 2003, H.R. 1, 108th Cong. § 1121 (2003) (passed in the House on June 27, 2003). Another bill in the 108th Congress would have permitted re-importation from the EU as well. Save Our Seniors Act of 2003, H.R. 2769, 108th Cong. § 2 (2003).

[307] Pharmaceutical Market Access Act of 2003, H.R. 2427, 108th Cong. (2003).

[308] Medicare Prescription Drug Improvement and Modernization Act of 2003, 21 U.S.C. § 804 (2004); Lueck, *supra* note 281, at A10. A subsequent Administration could certify safety and cost-effectiveness and begin importation from Canada without additional Congressional legislation.

[309] Henry J. Aaron, *Should Public Policy Seek to Control the Growth of Health Care Expenditures?*, Health Affairs W3-28 - 31 (Web Exclusive, Jan. 8, 2003) *available at* http://www.healthaffairs.org. ("The chances that we will adopt the Canadian or French health care system as a whole are about as good as those that we will join the British Commonwealth or adopt French as a second national language. Even adopting elements of foreign systems is problematic because important aspects of health care financing and delivery are mutually interrelated."). John Calfee of the American Enterprise Institute makes the point that reimportation of pharmaceuticals from Canada is equivalent to importing Canadian price controls. Calfee, *supra* note 279.

[310] Linda Temple, *Who Gets to Prescribe? Psychologists Send Drug Orders to Canada, Spark a Medical Debate*, USA Today, Dec. 18, 2003, at 10D.

competitive analysis of regulatory structures and allows market participants to influence the debates with diminished intermediation by interest groups.[311]

3. Virtual Arbitrage

The closely-related concept of virtual arbitrage involves foregoing the actual importation of drugs, but using lower observed prices as an external reference price, whether by government regulation or in contract. The US employs a virtual arbitrage system in requiring certain discounts for drugs purchased under Medicaid, discounts which reference other 'best' prices.[312] The West Virginia House of Delegates recently passed a bill which adopts the Federal Supply Schedule as a price cap for drug purchases by the State.[313] If West Virginia succeeds, expect many other States to follow suit.

Virtual arbitrage is preferred in any situation where physical arbitrage is acceptable. Virtual arbitrage is more efficient than physical arbitrage, since resources are not expended in transporting products or in policing against diversion.[314] Virtual arbitrage is also safer than physical arbitrage since the supply chain is not needlessly articulated through intermediaries. Just as in physical arbitrage, virtual arbitrage from low-income countries into OECD markets must be blocked if differential pricing is to be supported for essential medicines.[315] For this reason, several commentators have advised that OECD countries should not use low-income country differential prices as external reference prices in their domestic drug pricing regimes.[316]

Without clear data on patent rent optimality, no conclusion can be reached as to whether other forms of virtual arbitrage harm innovation. All arbitrage, whether virtual or not, will reduce the surplus captured by the patent holder and shift surplus to the consumer

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[311] Alvarez and Trachtman note that regulatory arbitrage may or may not have positive effects, depending upon the condition of spillovers (negative externalities). Jose E. Alvarez & Joel P. Trachtman, *Institutional Linkage: Transcending "Trade and …",* 96 Am. J. Int'l L. 77, 84 (2002) *citing* Joel P. Trachtman, *Regulatory Competition and Regulatory Jurisdiction,* 3 J. Int'l Econ. L. 331 (2000). In the present case, pharmaceutical regulatory arbitrage is a response to the existing free rider problem of national drug price regulation. This response may well destabalize the system, and force OECD countries to re-allocate jurisdiction on drug price regulation. Efficient re-allocation of jurisdiction is the primary theme in Alvarez and Trachtman's article. Alan O. Sykes remarks that subjecting domestic regulatory systems to the pressures of global trade "need not be unfortunate. International regulatory competition may well drive out foolish and wasteful regulations rather than undermine valuable regulations." Alan O. Sykes, International Trade and Human Rights: An Economic Perspective 17 (Univ. of Chicago John M. Olin Law & Economics Working Paper No. 188, 2d Series, May 2003).

[312] 42 U.S.C. § 1396r-8 (2004) (using reference prices to calculate drug prices and drug rebates under Medicaid).

[313] West Virginia Pharmaceutical Availability and Affordability Act, H.B. 4084, 2004 Reg. Sess. (W.V. 2004) (passed the House of Delegates Jan. 23, 2004; bill pending in Senate).

[314] On the issue of the transaction costs of physical arbitrage, *see* the comments by Harvey E. Bale, Jr., the Director-General of the International Federation of Pharmaceutical Manufacturers Associations, in Harvey E. Bale, Jr., *The Conflicts Between Parallel Trade and Product Access and Innovation: The Case of Pharmaceuticals*, 1 J. Int'l Economic L. 637 (1998). These claims are hotly disputed by proponents of parallel trade in pharmaceuticals. West & Mahon, *supra* note 201.

[315] The same condition holds for physical arbitrage, as discussed previously. *See supra* Section IV.C.3.

[316] *See supra* Sections IV.C.1 and V.F.1 for discussion of this point.

and the arbitrageur; however it begs the question to assume that arbitrage will reduce patent rents to a sub-optimal level. One should not assume that the externality is negative. It is possible that West Virginia's use of the Federal Supply Schedule retains supra-optimal innovation incentives while dramatically lowering the State's costs and improving access.

B. The Response to Canadian-US Arbitrage

The profitability of the pharmaceutical research industry depends in large measure on the present global differential pricing system. The current efforts to hinder Canadian arbitrage include legal interdiction, increasing transaction costs, and selectively controlling drug supplies shipped to Canada.

1. Reducing Arbitrage Demand

a. Legal Interdiction

If transaction costs are raised significantly, at some point the arbitrage transaction will become unrewarding and the market pressure on differential pricing will abate. For consumers, the transactions must be low-risk, particularly with regard to: (1) the legality of the transaction; (2) eligibility for reimbursement from third parties; and (3) counterparty risk of fraud.[317]

In the first two phases of Canadian arbitrage,[318] the transactions were clearly legal under US and Canadian law. The consumer physically visited a Canadian pharmacy, presented a valid prescription, and received the product. When returning to the United States, most Americans were not searched or questioned about their pharmaceuticals. Even if they had been scrutinized, the federal government allowed them to import small amounts of pharmaceuticals for personal use.[319]

When pharmaceutical arbitrage expanded to mail order and the internet, Canadian pharmacies and their agents emphasized the personal use exception. Prior to 2003, federal officials did not vigorously challenge this practice. Federal officials did not lack statutory authority to block importation through the mails or package delivery services,[320] but enforcement was uncommon. This lack of enforcement, coupled with the claims of legality under the personal use exception, permitted consumers to believe that the transaction was legal and the risk of government sanction was small.

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[317] Virtual arbitrage partially escapes this condition since no additional transportation costs are incurred and safety issues cannot be raised. Other transaction costs may still apply, such as the cost of observing prices and legal costs.

[318] *See supra* Section VI.A.

[319] The FDA's Personal Use Import Policy may be found at www.fda.gov/ora/import/pipinfo.htm.

[320] *See, e.g.,* United States v. Ramsey, 431 U.S. 606 (1977) (customs officials permitted to intercept mail for contraband).

Beginning in 2003, the enforcement environment changed.[321] Federal and state officials are currently attacking internet pharmaceutical arbitrage on multiple fronts. The FDA is aggressively enforcing against US companies involved in the trade.[322] The Customs Department has posted clarifications of the personal use exception to discourage importation.[323] Facilitators such as the Discount Prescription Center in West Virginia have been challenged by state Boards of Pharmacy as engaged in the unlicensed practice of pharmacy.[324] The FDA has sued facilitators such as Rx Depot for assisting in the importation of prescription drugs.[325] The FDA and state pharmacy investigators have also purchased prescription drugs in undercover operations.[326] Direct interdiction would include enforcement actions against consumers, but arresting grandparents for purchasing Canadian Lipitor is not politically viable.

b. Raising Information and Transaction Costs

These enforcement actions, while significant, have not shut down the arbitrage trade. From the perspective of arbitrage, the more significant element is pairing enforcement action with widespread publicity to dampen consumer demand. The effect is to increase consumers' transaction costs and deter arbitrage without comprehensive direct interdiction.

Raising information costs may also support product differentiation and discourage substitution.[327] Pharmaceutical arbitrage occurs when the consumer considers the drugs to be substitutable. These consumers are generally not trained medical specialists, and are unable to evaluate safety or efficacy.[328] These consumers are relying on the effectiveness of the Health Canada's Therapeutic Product Directorate (TPD), assuming that Canadian drugs are generally as safe as US drugs regulated by the FDA. If the safety or equivalence of drugs from Canadian internet pharmacies are in doubt, this assumption dissolves and risk averse consumers are less likely to arbitrage. Supporters of

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[321] Burton, *supra* note 266, at A1.

[322] Gardiner Harris and Monica Davey, *F.D.A. Begins Push to End Drug Imports*, N.Y. Times, Jan. 24, 2004; FDA News, *Recent FDA/U.S. Customs Import Blitz Exams Continue to Reveal Potentially Dangerous Illegally Imported Drug Shipments*, (Jan. 27, 2004) *available at* www.fda.gov; Lolita C. Baldor, *FDA: Too Costly to Legalize Drug Imports*, Las Vegas Sun, Dec. 24, 2003 (describing confiscations of illegal mail-order drugs in New York).

[323] U.S. Customs and Border Protection, Medication/Drugs (undated) *available at* http://www.cbp.gov/xp/cgov/travel/alerts/medication_drugs.xml (visited Feb. 15, 2004).

[324] The West Virginia Circuit Court issued a preliminary injunction forbidding enforcement by the West Virginia State Board of Pharmacy against Discount Prescription Center, concluding that Discount Prescription Center was not a pharmacy and did not violate state law. Carole Becker, d/b/a Discount Prescription Center v. West Virginia Board of Pharmacy, No. 03-C-1237, slip op. at 11-12 (Cir. Ct. Kanawha Co. Nov. 3, 2003).

[325] Rx Depot was shut down by a preliminary injunction granted by District Court Judge Claire V. Eagan on November 6, 2003. United States v. Rx Depot, Inc., No. 03-CV-0616-EA (M), slip op. at 2-4 (N.D. Ok. Nov. 6, 2003).

[326] Rx Depot Transcript, *supra* note 272, at 16-40.

[327] Philips, *supra* note 8, at ch. 12.

[328] Raising search costs for these consumers should hinder arbitrage and support differential pricing. *See* Philips, *supra* note 8, at ch. 12.

importation take the opposite tact. In October, 2003, the State of Illinois released a major report in support of importing patented drugs from Canada. The report concluded that the Canadian drug supply was actually safer than the US.[329]

A major component of the assault on pharmaceutical arbitrage has been to question safety and equivalence. The FDA has publicly announced its lack of confidence in the internet drug supply chain. Undercover operations and enforcement activities have highlighted the seizure of mislabeled, counterfeit or out of date drugs.[330] Questions have been raised as to whether the drugs are produced and transported under FDA standards of safety.[331] Labeling issues, such as the Canadian label for Accutane, have been identified.[332] The actual source of arbitraged drugs has also been publicly challenged by FDA officials who muse whether the drugs actually come from Canada at all; perhaps the true source is Thailand or India.[333]

At one level, these accusations prove too much. Counterfeit and unsafe drugs are found in the US market generally, and are not confined to the internet supply chain.[334] The FDA does not want to undermine consumer confidence in the US drug supply, but to distinguish the US domestic supply from international internet sources. Thus, the FDA opposes all international pharmaceutical arbitrage into the US.

c. The Special Case of Re-importation

Questions about production safety, equivalence, and labeling are reduced for a segment of this market known as *re-importation*. As a matter of production efficiency, pharmaceutical companies do not build plants in every country of the world. Many are located in the United States, including Puerto Rico, where the US government has long encouraged pharmaceutical research and production through generous tax incentives under Section 936 of the Internal Revenue Code.[335] Many drugs produced in these US plants are both sold into the US market as well as exported to nations like Canada. When these drugs make the return trip back to the US, the process is called *re-importation*.

Concerns about production safety, equivalence, and labeling of re-imported drugs should be carefully scrutinized. The Canadian government is fully satisfied that these drugs are

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[329] Kamath & McKibbin, *supra* note 264, at 11-16 (finding Canadian and US systems equivalent for most aspects, but finding the Canadian system superior in preventing the introduction of counterfeit drugs and incident reporting for internal process errors).

[330] *See, e.g.*, FDA News, Recent FDA/U.S. Customs Import Blitz Exams Continue to Reveal Potentially Dangerous Illegally Imported Drug Shipments (Jan. 27, 2004) *available at* http://www.fda.gov.

[331] Rx Depot Transcript, *supra* note 272, at 16-158.

[332] Rx Depot Transcript, *supra* note 272, at 77, ln. 22 (cross-examination of Melvin Frank Szymanski, consumer safety officer, FDA); Discount Prescription Center

[333] Hubbard, *supra* note 261 (noting one instance of a Canadian website shipping an Indian drug); *Savings Immense on Canadian Drugs*, Wash. Post, Nov. 5, 2003 ("It is not an answer to this problem to say go buy drugs from Canada, which may be coming from Pakistan and India and China and all those countries we have health concerns about") (Sen. John B. Breaux, D-La).

[334] Daniel Yee, *CDC: Seniors Prescribed Dangerous Drugs*, Las Vegas Sun, Feb. 9, 2004; *'Lipitor' Surfaces in Counterfeit Probe*, Wall St. J., Dec. 8, 2003, at B8.

[335] 26 U.S.C. § 936 (2004) (the Puerto Rico and Possessions Tax Credit).

safe, efficacious and properly labeled for Canadian use. The FDA worries about errors in shipping and handling from Canada to the consumer,[336] but these questions are relevant to all mail order pharmaceuticals and are not endogenous to pharmaceutical arbitrage from Canada. The FDA correctly notes that some Canadian standards differ from FDA rules, and forbids re-importation solely on that basis.[337] But the missing element is any showing that the Canadian drug supply is less safe. At the Rx Depot trial, the FDA did not assert that Canadian drugs were unsafe or had injured Americans.[338]

The most thorough recent analysis of this question concludes that the Canadian drug supply is actually safer on balance than the US. The State of Illinois report recommends a controlled importation system, with extensive safety checks, that results in a high quality drug supply at substantial savings.[339] The EU has many years of experience with parallel trade in pharmaceuticals, without significant safety issues.[340]

2. Reducing Arbitrage Supply and Demand

Each arbitrage transaction lowers the average price. If the supply or demand of product available for arbitrage can be limited, the net financial impact on the producer will be less severe. Conversely, if supply and demand are unlimited, differential pricing will disappear, and a new equilibrium price will prevail in both markets, shifting surplus from the producer to the consumer.

a. Targeting Canadian Internet Pharmacies

Pharmaceutical companies have identified Canadian pharmacies which sell to the US market. These pharmacies have been threatened with a refusal to deal unless the cross-border sales cease.[341] This threat not only cuts off the supply for the patented drugs being arbitraged, but it also uses the entire product line as a weapon to enforce differential pricing.

This strategy may not wholly prevent arbitrage. Some doubt the effectiveness or legality of attempts to restrict supply to Canada.[342] Members of Congress have asked the US

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[336] Rx Depot Transcript, *supra* note 272, at 29-31.
[337] Rx Depot Transcript, *supra* note 272, at 28, 76-77.
[338] Rx Depot Transcript, *supra* note 272, at 138-141; *but see* Hubbard, *supra* note 261 (claiming that internet sales from Canada will be more open to counterfeiting).
[339] Kamath & McKibbin, *supra* note 264, at 1-5.
[340] West & Mahon, *supra* note 201.
[341] Carlisle, *supra* note 273, at A9; Pugh, *supra* note 273; John O'Connor, *Canadians Warn of Rx Shortage*, Chi. Sun-Times, Nov. 13, 2003, *available at* www.suntimes.com; Simon, *supra* note 275; Tamsin Carlisle, *Pfizer Pressures Canadian Sellers of Drugs to U.S.,* Wall St. J. Jan. 14, 2004, at A6. Similar restrictions have been employed for many years to hinder parallel trade in Europe, Maskus & Ganslandt, *supra* note 17, at 69-70, with limited effectiveness. West & Mahon, *supra* note 201. For the effects of the same tactic on a national level, *see* Danzon, et at., *supra* note 165.
[342] Kamath & McKibbin, *supra* note 264, at 22 ("we do not feel the manufacturers rhetoric to restrict supply will ever materialize either broadly or consistently, and not at all in the Canadian pharmacies that are hybrid – internet and retail for two reasons. First limiting supply to Canadians pharmacies may risk their Canadian patent protection; second, as the Minnesota Attorney General and Illinois Attorney General

Attorney General to investigate whether antitrust laws are being violated,[343] and traditional Canadian pharmacies are complaining about the impact of drug company restrictions on their domestic operations.[344]

Canadian pharmacies will still be able to purchase drugs for export, but will be forced to purchase through intermediaries. Expenses and marginal cost are likely to rise, but given the significant price differentials between the US and Canada, arbitrage opportunities will remain. Perverse effects should also be noted. By cutting off direct supplies to exporting pharmacies, the pharmaceutical companies force additional intermediaries into the supply chain, which increases safety and handling problems, increases inefficiencies, and increases the opportunity for spoilage and introduction of counterfeits.[345] If the concern is truly for patient safety, supply restrictions are a crude and counterproductive tool.

b. Reducing Demand in the US With a Medicare Prescription Drug Benefit

Pharmaceutical companies also restrict demand in the US. The current market is mostly non-emergency outpatient drugs. For the Medicare population, these drugs have not been covered. If Medicare provided an outpatient drug benefit, a large part of the consumer arbitrage demand would disappear. In 2003, the pharmaceutical lobby reversed its historic opposition to a Medicare drug benefit, and embraced a market-based third party reimbursement plan in Medicare for outpatient drugs.[346] The new Medicare drug benefit will reduce consumer demand for arbitrage in an important population and thus maintain differential pricing.

C. Implications of Optimality for Canadian-US arbitrage

Mindlessly blocking pharmaceutical arbitrage within the OECD needlessly sacrifices cost and financial access on the altar of quality. Wonder drugs are useless if they are too expensive to be taken as prescribed. The government's regulatory power should not be used to force consumers into grey markets.

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are currently investigating any concerted effort by the pharmaceutical companies to limit supply may violate US antitrust laws.")

[343] Gardiner Harris, *Some in Congress Seek Inquiry Over Drug Supply to Canada,* N.Y. Times, Nov. 1, 2003.

[344] Carlisle, *supra* note 273, at A9; Pugh, *supra* note 273; O'Connor, *supra* note 316.

[345] Kamath & McKibbin, *supra* note 264, at 11-18 (Canada's drug distribution system does not rely on intermediates to the same extent as the US system. Increasing reliance on intermediates increases the risk of counterfeit drugs.).

[346] Prescription Drug and Medicare Improvement Act of 2003, 42 U.S.C. 1395 et seq. [§§ 1860D-1860D-26 of SSA] (2004). This plan also sows the seeds of future government price controls. Once the federal government becomes the payor, price increases are directly translated into budget issues. Medicare providers such as physicians and hospitals were once paid on a fee for service market basis; after years of budgetary issues, Medicare now imposes price controls and rate setting for physician and hospital services. Pharmaceuticals may well follow the same trend line.

The US should permit safe pharmaceutical arbitrage, particularly with countries with DRAs similar to the FDA. Regulatory resources would be devoted to coordination with these governments to ensure the integrity of the supply chain. With government support or neutrality, arbitrage would reduce US drug prices as differential pricing between OECD nations dissolved. Erosion of differential pricing would lower costs and improve financial access to important drugs.

The pharmaceutical companies bemoan this approach as destructive of long-term research incentives. This is an overly simplistic assessment, for it assumes that patent rents would be sub-optimal at undifferentiated OECD prices. But three other conditions are possible: (1) Current Canadian[347] prices are supra-optimal;[348] (2) Optimal patent rents would be achieved at prices between current US and Canadian prices; and (3) Companies will compensate for reduced unit prices without harming innovation.

First, if Canadian prices currently result in supra-optimal patent rents, then extending Canadian prices to the US will do no harm to innovation. This astonishing possibility would greatly reduce US pharmaceutical access issues without any decline in innovation. Price controls in Canada do not appear to have stifled innovation, as Canadian pharmaceutical R&D is robust and growing.[349]

Second, if one assumes that optimality lies somewhere between US and Canadian prices, then US prices could be decreased by some amount without harming innovation.

Third, the Canadian experience suggests that pharmaceutical research companies will react to reduced unit prices by stimulating demand for their products. In Canada, despite stable to declining Canadian unit prices for patented pharmaceuticals, national drug expenditure per capita is up at 10.2% annual growth rates. [350] Companies increase their profits in declining unit price markets by increasing unit sales,[351] and developing new drugs.[352] It may be possible to reduce prices, increase access and improve human health simultaneously – the Holy Grail of health policy.

The major barrier to empirically proving any of these three conditions is the lack of independent and reliable data on actual R&D expenditures and profits. Erosion of the OECD internal differential pricing system would put the ball in the pharmaceutical companies' court to demonstrate whether the resulting patent rents were globally sub-optimal. For perhaps the first time, these decisions could be made on the basis of actual data, rather than imprecise estimates.

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[347] Or non-US OECD country.
[348] Thanks to Professor James Friedberg for this suggestion.
[349] Barrados, et al., *supra* note 86, at ¶ 17.11 (Canadian drug companies agreed to increase R&D to 10% of sales by the end of 1996). For current data on Canadian pharmaceutical R&D, *see* http://www.canadapharma.org (the official trade association website).
[350] Canadian Institute for Health Information, *supra* note 24, at fig. 19 (stable to declining Patented Medicine Price Index since the introduction of the Patented Medicine Prices Review Board).
[351] Canadian Institute for Health Information, *supra* note 24, at fig. 13 (annual growth rate of per capita prescribed drug expenditures of 10.2% 1997-2000).
[352] Canadian Institute for Health Information, *supra* note 24, at 33-43.

VII. Conclusion

The head of the US global AIDS effort is Ambassador Randall Tobias, the former CEO of Eli Lilly & Co. When asked about the essential medicines access issue, he claimed it was "yesterday's issue" and that "from a price point of view, there's no longer that much difference."[353] I beg to differ. Not only are ARVs still not widely available at marginal cost for the 3 by 5 Initiative,[354] but drug pricing remains unaffordable for other global diseases such as cancer and heart disease in low-income nations. The industry prefers to turn off the media spotlight and assume the problems were fixed at Doha and Cancun. Meanwhile, global public health catastrophes continue to mount. For some of these conditions, we possess effective therapies which can be provided at a modest cost, but are withheld from the poor because of IP laws.

Health care public policy should not be chained to innovation, but must also champion access and cost. The heuristic device of globally optimal patent rents suggests that pharmaceutical access may be greatly improved, at a modest cost, without damaging optimal innovation.

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[353] Robin Wright, *A CEO to Direct the AIDS Battle: Former Eli Lilly Chief Comes Out of Retirement*, Washington Post, Feb. 13, 2004, at A25.

[354] The 3 by 5 Initiative will attempt to link many partners to treat 3 million people with ARVs by 2005. World Health Organization, The 3 by 5 Initiative, www.who.int/3by5/en. Funding is one limiting factor in this effort, so lowering the unit prices of ARVs will improve the chances of reaching the goal. Even if the goal is met, at least 3 million persons needing treatment will remain untreated in the low-income world. WHO, Fifty-Seventh World Health Assembly, Scaling Up Treatment and Care Within a Coordinated and Comprehensive Response to HIV/AIDS, WHA57.14 (May 22, 2004) (noting that 6 million people in developing countries need ARV treatment).