Pharmaceutical Arbitrage: Balancing Access and Innovation in International Prescription Drug Markets

Kevin Outterson, J.D., LL.M.*

INTRODUCTION

The price of prescription drugs lies at the heart of two major public health issues: distributing antiretroviral medicines for use against the global AIDS epidemic and purchasing medications from Canada by U.S. consumers using the Internet. Both situations highlight the need to reduce financial barriers to access to medications, while maintaining incentives to promote pharmaceutical innovation.

For better or worse, the World Trade Organization's (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)[1] is a global nexus for drug access issues.[2] In TRIPS-related

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1. *See* Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, art. 27.1, LEGAL INSTRUMENTS–RESULTS OF THE URUGUAY ROUND vol. 31, 33 I.L.M. 81 (1994) [hereinafter TRIPS or TRIPS Agreement]. The United States implemented the WTO agreements in the Uruguay Round Agreements Act, Pub. L. No. 103-465, 108 Stat. 4809 (1994).

2. The story of how the WTO TRIPS Agreement became the de facto forum for these

discussions, two sets of arguments are usually forwarded. Some argue that pharmaceutical prices are necessarily high because innovation is expensive.[3] They posit that the research and development (R&D) enterprise must be nurtured by high prices to yield the next generation of breakthrough therapies.[4] Others counter that much of the profits going to pharmaceutical companies[5] are used for marketing and other expenses

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issues has been told by many authors. Among the best accounts are books by Peter Drahos and John Braithwaite, Susan Sell, and an article by Laurence Helfer. PETER DRAHOS WITH JOHN BRAITHWAITE, INFORMATION FEUDALISM: WHO OWNS THE KNOWLEDGE ECONOMY? (2002); SUSAN K. SELL, POWER AND IDEAS: NORTH-SOUTH POLITICS OF INTELLECTUAL PROPERTY AND ANTITRUST (1998); SUSAN K. SELL, PRIVATE POWER, PUBLIC LAW: THE GLOBALIZATION OF INTELLECTUAL PROPERTY RIGHTS (2003); Laurence R. Helfer, *Regime Shifting: The TRIPS Agreement and New Dynamics of International Intellectual Property Lawmaking*, 29 YALE J. INT'L L. 1 (2004).

3. *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, 102-04 (Brigitte Granville ed., 2002) [hereinafter ECONOMICS OF ESSENTIAL MEDICINES]. Dr. Bale is the Director-General of the International Federation of Pharmaceutical Manufacturers Association.

4. ANDY SCHNEIDER, TAXPAYERS AGAINST FRAUD EDUCATION FUND, REDUCING MEDICARE AND MEDICAID FRAUD BY DRUG MANUFACTURERS: THE ROLE OF THE FALSE CLAIMS ACT 47 (2003) ("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.").

5. In this Article, the terms "pharmaceutical companies" and "PhRMA companies" refer to the research-based pharmaceutical companies that are members of the PhRMA trade association. Pharmaceutical companies have traditionally been categorized as either research companies (e.g., Pfizer, Merck) or generic companies without significant research programs (e.g., Mylan Labs, Cipla Ltd.). The United States trade association of research pharmaceutical companies is the Pharmaceutical Research and Manufacturers of America (PhRMA). *See* Pharmaceutical Research and Manufacturers of America, *at* http://www.phrma.org (last visited Oct. 20, 2004). The international trade association of PhRMA company groups is the International Federation of Pharmaceutical Manufacturers Associations (IFPMA). *See* International Federation of Pharmaceutical Manufacturers, *at* http://www.ifpma.org (last visited Oct. 20, 2004). Generic drug companies have their own trade associations, such as GPhA, *at* http://www.gphaonline.com (last visited Oct. 20, 2004). 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 sometimes be more accurate to describe research or generic lines of business, rather than companies per se.

rather than for R&D[6] and that without affordable access, innovation is a cruel taunt.[7] New wonder drugs will not improve health unless patients are actually able to receive them. A pill you cannot afford is neither safe nor effective. Medicines, according to this argument, are not normal market goods to be distributed primarily to the wealthy.[8]

Nowhere are the arguments for the equitable distribution of medicines made with more force than in the AIDS treatment crisis. Differential pricing is one response to the tension between innovation and access with regard to AIDS medications: It permits antiretroviral drugs to be sold cheaply or donated in low income countries, while maintaining high prices in markets like the United States.[9] In theory, high prices in high income countries can support innovation, while lower prices in low income countries improve access. However, differences in pricing—and thus opportunities for arbitrage—do not always reflect direct or voluntary efforts to facilitate access in developing countries;[10] they may also result from diverse systems of government regulation and intervention and corporate efforts to maximize profit. The price of drugs is affected by domestic intellectual property (IP) laws, pharmaceutical reimbursement systems, and other legal systems specific to each country. As a result, for example, patented pills in Australia are often cheaper than their equivalents in Canada, which are in turn often cheaper than those in the United States. These pricing gaps create the demand for cross-border pharmaceutical parallel trade, or pharmaceutical arbitrage. It is alleged that if such trade is left unchecked, it will significantly reduce the financial gains reaped in certain countries, most prominently the United States,

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6. *See, e.g.*, Marcia Angell, *The Truth About Drug Companies*, N.Y. REV. BOOKS, July 15, 2004, at 51.

7. *See, e.g.*, 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, 29-30 (2002).

8. MÉDECINS SANS FRONTIÈRES, MSF CAMPAIGN BROCHURE 5 (2004), http://www.accessmed-msf.org/documents/campaignbrochure2004.pdf ("Medicines aren't just any consumer goods.").

9. A joint workshop was conducted in 2001 on differential pricing for essential drugs by the World Health Organization and the World Trade Organization, with substantial participation from global drug companies. The final report is published as WORLD HEALTH ORG., REPORT OF THE WORKSHOP ON DIFFERENTIAL PRICING AND FINANCING OF ESSENTIAL DRUGS: A WHO/WTO SECRETARIAT WORKSHOP (2001), http://whqlibdoc.who.int/hq/2001/a73725.pdf. A more concise summary of the final report was published in 2002. WHO-WTO, *Differential Pricing and the Financing of Essential Drugs*, *in* ECONOMICS OF ESSENTIAL MEDICINES, *supra* note 3, at 209-31.

10. This is sometimes referred to in this Article as voluntary differential pricing.

which provide financial support for global R&D innovation[11] and, thus, may undermine voluntary differential pricing schemes (e.g., AIDS initiatives) that benefit low income countries.[12] So long as R&D costs continue to be partially funded by sales revenues,[13] the conventional wisdom holds that pharmaceutical arbitrage is a major threat to both differential pricing and innovation. Preventing pharmaceutical arbitrage from low income markets into high income markets is generally viewed as the linchpin of this analysis.

Thus, in the context of differential pricing, pharmaceutical arbitrage is becoming an increasingly prominent subject of debate; in particular, fear of arbitrage is being used to justify expanding pharmaceutical IP rights and related powers of appropriation.[14] This Article explores key functions of pharmaceutical arbitrage, including its impact on access and innovation and its implications for the implementation of the TRIPS Agreement and other government interventions affecting pharmaceutical prices and distribution.

Part I of the Article establishes a theoretical framework for understanding pharmaceutical markets and innovation, using the heuristic device of *optimal pharmaceutical rents* to explore pharmaceutical arbitrage.[15]

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11. Tom Blackwell, *Canada's Drug Pricing Unfair, U.S. Alleges: Pharma Companies Back Plan To Restrict Cross-Border Sales*, NAT'L POST (TORONTO), May 3, 2004, at A6; Gardiner Harris, *Cheap Drugs from Canada: Another Political Hot Potato*, N.Y. TIMES, Oct. 23, 2003, at C1. *But see* ALAN SAGER & DEBORAH SOCOLAR, DO DRUG MAKERS LOSE MONEY ON CANADIAN IMPORTS? (Boston Univ. Sch. of Pub. Health, Data Brief No. 6, 2004), http://www.healthreform program.org.

12. PATRICIA M. DANZON & ADRIAN TOWSE, DIFFERENTIAL PRICING FOR PHARMACEUTICALS: RECONCILING ACCESS, R&D AND PATENTS 28-29 (AEI-Brookings Joint Ctr. for Regulatory Studies, Working Paper No. 03-7, 2003).

13. A prominent alternative formulation would be the Hubbard-Love R&D Treaty, which does not rely on retail sales to recover R&D costs. Tim Hubbard, Alternatives to the Price System, Presentation at Columbia University (Dec. 4, 2003), *at* http://www.earthinstitute.columbia.edu/cgsd/accesstomedicines_papers.html; James Love, A New Trade Framework for Global Healthcare R&D, Presentation at Columbia University (Dec. 4, 2003), *at* http://www.earthinstitute.columbia.edu/cgsd/accesstomedicines_papers.html.

14. Powers of appropriation are those mechanisms, including legal rights and entitlements, that allow individuals or entities to control the distribution of (and thus to capture) the value created. *See, e.g.*, David Ellerman, Introduction to Property Theory (Apr. 2004) (unpublished manuscript, on file with the *Yale Journal of Health Policy, Law, and Ethics*), http://www.economics.ucr.edu/seminars/spring04/Intro-to-Prop-Theory.pdf.

15. In this Article, the term *rents* is generally used in lieu of *patent rents* because in pharmaceutical markets, many legal tools are utilized to make returns on investment appropriable to the innovator in addition to patent law. *See infra* Section I.C. The phrase

In the absence of definitive data on pharmaceutical R&D, the heuristic can offer a guide to policymakers attempting to balance access and innovation. Part II of the Article applies this framework to two situations: the global pricing of antiretroviral drugs and the issue of Canadian-U.S. cross-border arbitrage.

The primary conclusions of this Article fall into two clusters. First, the heuristic indicates that several forms of pharmaceutical arbitrage are beneficial, delivering lower prices to consumers without harming innovation. Arbitrage within and between high income markets, such as the Canadian Internet sales to the United States, will not harm innovation if pharmaceutical rents remain supra-optimal. Pharmaceutical industry claims of sub-optimality must be backed with full transparency to allow for public evaluation of pricing, production cost, and profitability data throughout the world.

More broadly, the heuristic indicates that optimal economic incentives for innovation can be maintained while providing low income populations with greatly expanded access to patented medicines. Unlike physical property, pharmaceutical innovation is generally nonrival.[16] Therefore, in markets which are unlikely to contribute importantly to global pharmaceutical rents, the shackles of intellectual property law and other forms of appropriation are both unnecessary and dangerous; such laws should be set aside in these circumstances, permitting the broadest possible dissemination of pharmaceutical innovation. Practical experience suggests that voluntary differential pricing is unlikely to deliver needed medications at the lowest possible marginal cost.[17] Low transaction cost compulsory licenses are preferable and are consistent with the needs for innovation.[18]

Furthermore, while much of the current debate is focused on AIDS (and to a lesser extent on tuberculosis and malaria), the analysis in this Article is not limited to these conditions. Consistent with global optimal pharmaceutical rents, access can be expanded to all categories of global diseases, including cancer and heart disease, without damaging innovation.

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pharmaceutical rents is thus meant to capture all of the various ways, including regulation-based market exclusivity, in which pharmaceutical innovators appropriate rents. When the term *patent rents* is used herein, the narrower meaning is intended.

16. Nonrival goods can be utilized simultaneously by multiple users without risk of exhaustion. *See* JOHN B. TAYLOR & IMAD MOOSA, MACROECONOMICS (2d ed. 2002). For further discussion of this term, see *infra* text accompanying note 24.

17. *See infra* note 151 and accompanying text.

18. The need to improve compulsory licensing procedures is discussed in Part II.

In the second cluster of conclusions, I determine that the threat of pharmaceutical arbitrage is overstated and rarely observed empirically. This Article describes the legal and commercial frameworks which generally obstruct arbitrage, and argues that the most dangerous threat to innovation and public health comes from counterfeit medications, not from arbitrage. Resources now being expended to limit diversion in donor programs and differential pricing schemes could be more profitably reallocated to anti-counterfeiting initiatives within high income markets. A prime example of a misdirected anti-arbitrage effort is the initiative within the President's Emergency Plan for HIV/AIDS Relief (PEPFAR) to establish its own supply chain and procurement policies.

I. THE THEORY OF PHARMACEUTICAL ARBITRAGE

A. The Innovation Theory of IP Law

From ancient times, law and social conventions have supported the right to exclude—a fundamental component of the concept of personal and real property.[19] Persons investing in the production of goods are able to reap a reward for their efforts because, in part, the law creates a property right in the goods produced. This property right is somewhat exclusive, meaning that other persons cannot take the property without consent, due process, or some important public policy.[20] In the language of economics, goods and services are "appropriable."[21] At common law, knowledge was not considered personal property,[22] perhaps because the

19. *See, e.g., Exodus* 20:15 (NRSV) ("You shall not steal."). The right to exclude others from an individual's or group's real property developed much later and is not yet fully ascendant in some communities.

20. In physical property, the right to exclude is subject to many exceptions and conditions; critiques of analogies to intellectual property are yielding some interesting research. *See, e.g.*, MARK A. LEMLEY, PROPERTY, INTELLECTUAL PROPERTY, AND FREE RIDING 3-17 (John M. Olin Program in Law & Econ., Working Paper No. 291, 2004); STEWART E. STERK, WHAT'S IN A NAME? THE TROUBLESOME ANALOGIES BETWEEN REAL AND INTELLECTUAL PROPERTY 1-3 (Jacob Burns Inst. for Advanced Legal Studies, Benjamin N. Cardozo Sch. of Law, Working Paper No. 88, 2004).

21. Use of the term "appropriable" can be found in an array of works. *See, e.g.*, James J. Anton & Dennis A. Yao, *Expropriation and Inventions: Appropriable Rents in the Absence of Property Rights*, 84 AM. ECON. REV. 190 (1994).

22. *See, e.g.*, 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). *See also* Carle Hesse,

use of information is subject to at least two peculiar characteristics. First, knowledge is generally inappropriable or nonexcludible: It is typically more difficult to exclude other persons from using knowledge than physical property.[23] Second, knowledge is nonrival: While physical goods like corn or wheat are exhausted when used, knowledge may be used without exhaustion.[24]

The nonrival nature of knowledge permits its widest possible dissemination without creating shortages, a potential boon for humanity.[25] But, the fly in the ointment is appropriation. If *homo econimus* understands that the fruits of research will not be appropriable, then the market offers no financial incentive to innovate. Others will gladly use the innovation without compensating the innovator. The economic model predicts that when the innovator cannot capture the positive externality (or consumer surplus), the incentive to innovate is undermined.

However, this model is overly pessimistic. Inventive knowledge grew in the centuries prior to the adoption of patent law; important books were

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The Rise of Intellectual Property, 700 B.C. – A.D. 2000: An Idea in the Balance, DAEDALUS, Spring 2002, at 26-45 (tracing the epistemological foundations of intellectual property). The innovation theory is not the sole justification for patent law, but it is the dominant one in Anglo-American jurisprudence. Another possible 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. *See* Vincenzo Denicolo & Luigi Alberto Franzoni, *The Contract Theory of Patents*, 23 INT'L REV. L. & ECON. 365, 366-68 (2004). In pharmaceuticals, the marketing approval process requires disclosure in any event, making the contract theory less applicable.

23. This Article uses the terms inappropriable and nonexcludible interchangeably.

24. While knowledge is not destroyed through use, it may lose value because it is inappropriable. For example, market-moving financial information loses its value quickly, particularly as market participants act on the information. This is a function of inappropriability, rather than exhaustion or rivalry. From a societal perspective, knowledge does not lose value through use, but adds to the public domain.

25. The point is occasionally overlooked. In his critique of the consequences of the TRIPS Agreement, for example, Alan Sykes underemphasizes 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 CHI. J. INT'L L. 47, 56 (2002); *see also* William M. Landes & Richard A. Posner, *Indefinitely Renewable Copyright*, 70 U. CHI. L. REV. 471, 484-86 (2003) (arguing that some forms of IP are rival, particularly trademarks and personal likenesses). Trademarks and personal likenesses indicate origin rather than being knowledge per se. Pharmaceutical knowledge is nonrival in the classic sense, although nonrival use will certainly undercut monopoly pricing and affect *ex ante* innovation incentives.

written before the Statute of Anne.[26] This can at least be partially explained by non-economic motives for research, such as curiosity or personal achievement.[27] In most industries, patents play a relatively minor role in promoting innovation.[28]

Nevertheless, pharmaceutical research companies strongly embrace this neo-classical innovation model.[29] They argue that without IP laws first

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26. The British Statute of Anne is considered the first copyright law. Statute of Anne, 1710, 8 Ann., c. 19 (Eng.). Today's industrialized countries are relatively recent converts to the cause of strong IP laws. DRAHOS WITH BRAITHWAITE, *supra* note 2, at 29-38.

27. The open source movement in science is built upon such factors, as articulated by several leading scientists. Tim Hubbard & James Love, *Medicines Without Barriers: From the Human Genome Project to Open Development Models for Medical R&D*, NEW SCIENTIST, June 14, 2003, at 29; Stephen M. Maurer et al., *Finding Cures for Tropical Diseases: Is Open Source an Answer?*, *in* BIOTECHNOLOGY: ESSAYS FROM ITS HEARTLAND 33-37 (Lynn Yarris ed., 2004), http://www.salilab.org/publications; Sir John Sulston, Open and Collaborative Movements in Science, Presentation at the Trans-Atlantic Consumer Dialogue Future of WIPO Workshop, Geneva (Sept. 13, 2004).

28. For most industries, it appears that patents play a relatively modest role in making invention non-appropriable by free riders. *See, e.g.*, ASHISH ARORA ET AL., R&D AND THE PATENT PREMIUM 4, 34-35 (Nat'l Bureau of Econ. Research, Working Paper No. 9431, 2003) ("Empirical work also suggests that the inducement provided by patents for innovation is small."); WESLEY M. COHEN ET AL., PROTECTING THEIR INTELLECTUAL ASSETS: APPROPRIABILITY CONDITIONS AND WHY U.S. MANUFACTURING FIRMS PATENT (OR NOT) 2, 24-25 (Nat'l Bureau of Econ. Research, Working Paper No. W7552, 2000) (finding that forty years of empirical data demonstrates that patents do not improve innovation, with exceptions in pharmaceuticals, and concluding that patents are not the most significant mechanisms for appropriating returns to innovation in most industries, with secrecy, lead time, and complimentary capabilities leading); 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); Richard C. Levin, *A New Look at the Patent System*, 76 AM. ECON. REV. 199, 200-01 (1986); Edwin J. Mansfield, *Patents and Innovation: An Empirical Study*, 32 MGMT. SCI. 173 (1986). In pharmaceuticals, secrecy is not an option with the public drug application process, and the evidence strongly suggests a link between patents and innovation. ARORA ET AL., *supra*, at 4-5, 35. Arora's study found a significant patent premium (i.e., a positive return on investment), particularly in biotechnology, medical instruments, and drugs. *Id.* at 30, 34-35.

29. One prominent source on R&D expenditures by PhRMA companies is Joseph A. DiMasi et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151 (2003). These claims are defended vigorously by PhRMA and its members. *See, e.g.*, ERNST & YOUNG LLP, PHARMACEUTICAL INDUSTRY R&D COSTS: KEY FINDINGS ABOUT THE PUBLIC CITIZEN REPORT (2001), http://www.phrma.org/mediaroom/press/release//2001-08-11.277.pdf; Sidney Taurel, *Hands Off My Industry*, WALL. ST. J., Nov. 3, 2003, at A14. Sidney Taurel is the president, chairman, and chief executive officer of Eli Lilly.

movers would incur all research costs (including failed programs), while free riders (subsequent movers such as generic drug companies) would benefit from significantly lower cost structures.

IP law offers an allegedly second-best solution[30] to this impasse—the Constitution's favorite monopolies "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."[31] Currently, under U.S. federal law and the TRIPS Agreement, the patent period is not less than twenty years after filing.[32]

The social costs of making pharmaceutical knowledge appropriable are generally three-fold. First, the cumulative effect of these laws allows the

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30. *See, e.g.*, TOMAS J. PHILIPSON & STÉPHANE MECHOULAN, INTELLECTUAL PROPERTY & EXTERNAL CONSUMPTION EFFECTS: GENERALIZATIONS FROM PHARMACEUTICAL MARKETS 3 (Nat'l Bureau of Econ. Research, Working Paper No. 9598, 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."); *id.* at 8, 14-15. For a timely recognition that a bare patent does not equal the clear right to exclude, see Mark A. Lemley & Carl Shapiro, *Probabilistic Patents*, J. ECON. PERSP. (forthcoming 2004) (manuscript at 19, on file with author). Lemley and Shapiro's analysis is not specific to pharmaceuticals, where multiple patents and other appropriation strategies heighten the degree of exclusion. *See infra* Part I.

31. U.S. CONST. art. I., § 8, cl. 8. Of course, 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 STUD. 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.

32. 35 U.S.C. § 154 (2000); TRIPS, *supra* note 1, art. 33. TRIPS permitted many developing countries to implement on a delayed basis. TRIPS, *supra* note 1, arts. 65-66. After extensions, most developing countries must implement the TRIPS Agreement by January 1, 2005, but the thirty "least developed countries" may defer full implementation for pharmaceutical products until 2016. *Declaration on the TRIPS Agreement and Public Health*, Doha WTO Ministerial 2001, WT/MIN(01)/DEC/2, ¶ 7 (Nov. 20, 2001) [hereinafter *Doha Declaration on TRIPS*]. Despite these concessions, all but three of Africa's Least Developed Countries (LDCs) have already adopted patent laws for pharmaceuticals. PHIL THORPE, STUDY ON THE IMPLEMENTATION OF THE TRIPS AGREEMENT BY DEVELOPING COUNTRIES 1 (Comm. on Intellectual Prop. Rights, Study Paper 7 (circa 2004). TRIPS merely sets minimum periods of IP protection; the United States can still unilaterally extend patent protection, and has done so with copyright. WTO Members are also free to negotiate so-called "TRIPS-plus" agreements with additional provisions requiring protections in excess of the TRIPS Agreement's minimum standards.

innovator to charge a higher price under monopolistic conditions. James Love, Director of the Center for Consumer Project on Technology, estimates the deadweight cost at $400 billion per year.[33] Second, these higher prices hinder medical access, directly impacting the health of many low income people globally.[34] Finally and most generally, appropriation, by necessity, delays the entry of knowledge into the public domain and thus may hinder cumulative innovation.[35]

The perceived tension between the development and dissemination of knowledge permeates the most compelling issues in pharmaceutical IP policy. Patent doctrines such as scope,[36] experimental use,[37] and fair use[38] are also battlegrounds in the struggle between innovation and the public domain.[39] This Article locates additional laws in the policy battleground as well. If too many laws support appropriation (i.e., excessive IP rights and other excessive restrictions on nonrival use), the system needlessly raises costs and restricts access to important pharmaceuticals.[40] Too few might throttle the R&D enterprise, and society might forgo valuable qualitative improvements. It is far from clear that current policy strikes an appropriate balance. At the celebration of the tenth anniversary of the TRIPS

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33. James Love, Statement of Essential Inventions, Inc. to the Commission on Intellectual Property Rights, Innovation and Public Health (Apr. 5, 2004).

34. *See infra* Subsection II.A.1.

35. *See infra* notes 130-131 and accompanying text.

36. Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839 (1990) (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.*, WILLIAM D. NORDHAUS, INVENTION, GROWTH, AND WELFARE: A THEORETICAL TREATMENT OF TECHNOLOGICAL CHANGE 70-90 (1969) [hereinafter NORDHAUS, INVENTION, GROWTH & WELFARE]; William D. Nordhaus, *The Optimum Life of a Patent: Reply*, 62 AM. ECON. REV. 428 (1972) [hereinafter Nordhaus, *The Optimum Life of a Patent*]; F.M. Scherer, *Nordhaus' Theory of Optimal Patent Life: A Geometric Reinterpretation*, 62 AM. ECON. REV. 422-27 (1972) [hereinafter Scherer, *Optimal Patent Life*]. For a recent example, see PHILIPSON & MECHOULAN, *supra* note 30, at 8-13.

37. Rebecca Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. CHI. L. REV. 1017 (1989); Rebecca Eisenberg, *Proprietary Rights and the Norms of Science in Biotechnology Research*, 97 YALE L.J. 177 (1987).

38. Maureen A. O'Rourke, *Toward a Doctrine of Fair Use in Patent Law*, 100 COLUM. L. REV. 1177 (2000).

39. Dam, *supra* note 31, at 261-68.

40. This point assumes that increased consumption of patented pharmaceuticals creates net positive externalities, i.e. that society benefits from increased access and consumption of the drug. PHILIPSON & MECHOULAN, *supra* note 30, at 9.

Agreement, Pascal Lamy, Director of DG-Trade, noted:

> IPRs are justified by their societal purpose: they constitute a public policy tool to encourage innovation and creativity. These are the ends, and the patents and copyrights granted to innovators and creators are the means to achieve it. But the hierarchy of ends and means does not end here. Indeed, the encouragement of innovation and creativity is itself serving higher purposes: economic, social and cultural development that should benefit all.
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> So, international intellectual property policy is a question of striking the right balance between private interests, their public policy objective (access to knowledge) and other public goods. Should this public/private bargain be struck in the same way in all WTO Members? Not necessarily. Here the level of development and the national public policy objectives come into play.[41]

B. Differential Pricing and Pharmaceutical Arbitrage

1. Differential Pricing

In simple economic models, goods are sold at a single market-clearing price. In reality, 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.[42]

Indeed, differential pricing is common: The same product is frequently sold at different net prices to various buyers.[43] The seller charges

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41. Pascal Lamy, The TRIPs Agreement 10 Years On, Speech to the International Conference on the 10th Anniversary of the WTO TRIPs Agreement (June 23, 2004), http://europa.eu.int/comm/commissioners/lamy/speeches_articles/spla233_en.htm.

42. 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 (2000). This Article follows the usage most common in the essential medicines literature: differential pricing. Tiered pricing, equity 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, 2002).

43. This particular definition is found in LOUIS PHILIPS, THE ECONOMICS OF PRICE

what each market segment will bear.[44] 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.[45] First-degree price discrimination is also known as perfect price discrimination, since it fully extracts all consumer surplus for the benefit of the producer.[46] In the case of pharmaceuticals, this would provide cash flow for innovation but would impair access through higher consumer cost. In reality, transaction costs almost always make first-degree differential pricing untenable: The seller's marginal costs of collecting and understanding all of the relevant factors for each buyer usually outweigh the gains in marginal revenue.[47] 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.[48] In second-degree price discrimination, purchasers segment themselves into price levels. For example, railroad passengers choose either first, second, or third class seats and coupon clippers segment themselves into distinct markets. 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 offer examples of both second- and third-degree price discrimination.[49]

DISCRIMINATION 6, 17 (1983).

44. The airline industry provides an oft-cited example. On almost every flight, passengers will have paid many different prices for the same service. The market has been segmented into multiple buyer groups, including business travelers, vacation travelers, frequent flyers, and last minute purchasers. *See, e.g.*, ERNST R. BERNDT, AM. ENTERPRISE INST. FOR PUB. POLICY RESEARCH, UNIFORM PHARMACEUTICAL PRICING: AN ECONOMIC ANALYSIS 5-6, 9-10 (1994). However, it is worth noting that some, like Louis Philips, argue 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. PHILIPS, *supra* note 43, at 9.

45. The classic description of first-, second-, and third-degree price discrimination is found in ARTHUR CECIL PIGOU, THE ECONOMICS OF WELFARE 321-47 (4th ed. 1920). A helpful summary of Pigouvian price discrimination may be found in PHILIPS, *supra* note 43, at 11-14.

46. It is perfect from the perspective of the selling firm, rather than the consumer. PHILIPS, *supra* note 43, at 158.

47. PIGOU, *supra* note 45, at 280.

48. *See* PIGOU, *supra* note 45; PHILIPS, *supra* note 43, at 12-13.

49. Examples of second-degree price discrimination include consumer selection of branded or unbranded drugs, the opportunity to apply for patient assistance programs, and monopsonistic price controls. Examples of third-degree price discrimination include voluntary differential pricing programs by manufacturers.

The primary focus of this Article is third-degree price discrimination, although I typically employ the more general term, differential pricing. The term "voluntary differential pricing" in this Article refers specifically to third-degree price discrimination, as distinguished from second-degree price discrimination such as price controls imposed by monopsonistic payor governments.

Differential pricing is endemic to pharmaceutical markets.[50] Pharmaceutical companies segment markets for differential pricing purposes, generally along efficient boundaries such as political borders or payor classes, with the support of legal institutions. Voluntary differential pricing exists among different countries[51] and among different buyers or payor classes within countries.[52] Second-degree differential pricing occurs when price controls are imposed.[53]

2. Pharmaceutical Arbitrage

Pharmaceutical arbitrage is the theoretical nemesis of differential pricing.[54] While differential pricing assumes that the first purchaser is the

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50. This is true, at least, in recent years. *See infra* Part II. But at least one Wall Street Journal editor is calling on PhRMA companies to abandon voluntary price discrimination for a single price in all developed countries. *See* Holman W. Jenkins Jr., *Two CEOs, Two Trials*, WALL ST. J., July 14, 2004, at A15 ("A better idea would be for Pfizer and fellow drug makers to publish and stick to a single price at which each drug will be sold to customers in the developed countries. Price discrimination may be socially beneficial; [i]t may allow more people to benefit from a new drug than would be possible if each had to pay an equal share of research costs. Politically, however, price discrimination has become an albatross around the industry's neck, because other developed nations use price controls to force R&D costs back onto American consumers.").

51. For example, in many African countries pharmaceutical companies charge less for certain drugs in than they do in the United States. *See, e.g.*, John S. James, *Merck, Bristol-Myers Squibb Announce Major Price Reductions in Poorest Countries*, AIDS TREATMENT NEWS, Feb. 26, 2001, http://www.aids.org/atn/a-361-03.html.

52. Examples in the United States include Medicare, Medicaid, Veterans Affairs, federal employees, private health plans, and individuals.

53. *See, e.g., infra* note 199 and accompanying text (discussing Australia's scheme).

54. For a classic account of the interplay between arbitrage and differential pricing, see PHILIPS, *supra* note 43, at 14-16. A recent study from the London School of Economics does not find any evidence of the predicted price convergence in pharmaceutical parallel trading markets in Europe. PANOS KANAVOS ET AL., THE ECONOMIC IMPACT OF PHARMACEUTICAL PARALLEL TRADE IN EUROPEAN UNION MEMBER STATES: A STAKEHOLDER ANALYSIS 15-16 (London Sch. of Econ. & Political Sci., Special Research Paper, 2004), http://www.lse.ac.uk/collections/LSEHealthAndSocialCare/documents/otherpaperseries.

ultimate user, arbitrage occurs when buyers in a lower-priced market re-sell the product to consumers in a higher-priced market. Pharmaceuticals sold for five dollars in India may be identical to products sold for one hundred dollars in the United States, creating the opportunity for arbitrage. When arbitrage involves IP and crosses an international border, it is called parallel trade.[55] Absent other constraints, neo-classical economic theory predicts that arbitrage will erode price-differentiated 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,[56] improving access through lower cost. Arbitrage is in fact a normal function of a competitive capitalistic economy, a key component of the invisible hand. Arbitrage loses favor when it threatens innovation by hindering appropriation by pharmaceutical companies. As will be seen later, the empirical reality of pharmaceutical arbitrage departs from the neo-classical model in significant ways.[57] This Article recognizes that pharmaceutical arbitrage may be either helpful or dysfunctional to consumer welfare.

C. Laws Affecting Pharmaceutical Arbitrage

Successful pharmaceutical price discrimination requires market segmentation and must minimize arbitrage by customers and intermediaries. Several tools may be employed, including contract, product differentiation supported by trademarks, and regulatory structures.[58] Each affects the degree of appropriation in pharmaceutical markets, and thus, the balance between access and innovation.

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55. 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 Pharmaceutical Products: Implications for Procuring Medicines for Poor Countries*, *in* ECONOMICS OF ESSENTIAL MEDICINES, *supra* note 3, at 57. The practice is not necessarily illegal, depending upon the country's laws concerning exhaustion of IP rights. *See supra* Subsection I.A.1.

56. PHILIPS, *supra* note 43, at 18.

57. *See infra* Subsection II.A.1; *see also* supra note 54 (citing study finding no empirical evidence of price convergence in EU pharmaceutical arbitrage).

58. *See* Jonathan M. Barnett, *Private Protection of Patentable Goods*, 25 CARDOZO L. REV. 1251 (2004).

1. Contract

Private ordering may support differential pricing: The contract between a buyer and seller may expressly or implicitly forbid arbitrage.[59] If the customer breaches the agreement, the seller can pursue contractual remedies. The effectiveness of contractual remedies will in many cases depend upon whether the seller has privity with every arbitrageur and on the monitoring costs required to ensure compliance. In pharmaceutical markets, manufacturers are likely to lack privity with the multiple layers of pharmaceutical distributors and retailers, and contracts of adhesion in the style of shrink-wrap licensing are impractical since pharmaceutical goods are sold rather than licensed. Contractual restrictions on subsequent trade may run afoul of competition law. The European Court of Justice, for example, is generally skeptical of contractual provisions preventing intra-European arbitrage.[60] Any relaxation of these competition law principles, or a novel expansion of licensing-style restrictions on subsequent transfer, would decrease the potential for arbitrage and expand the appropriation powers of pharmaceutical innovators.

2. Product Differentiation

Successful arbitrage requires that the lower priced product be the same as, or easily substituted for, the more expensive product. When the product is fungible and easily transferable, consumers can cross the price discriminating market segments by choosing the lowest price.[61] However, producers rarely concede strict fungibility; marketing efforts are deployed to influence consumers and reduce their willingness to make substitutions, thus supporting differential pricing.[62] This process generally occurs

59. Airlines, for example, forbid the transfer of tickets. Some firms refuse to sell equipment, but only lease it with sub-leasing forbidden. The famous example of leased Xerox equipment is described in PHILIPS, *supra* note 43, at 151-53. A more recent example is the software industry's widespread use of non-transferable licenses. These are most often clickwrap or shrink-wrap licenses—contracts of adhesion. *See* J.H. Reichman & Jonathan A. Franklin, *Privately Legislated Intellectual Property Rights: Reconciling Freedom of Contract with Public Good Uses of Information*, 147 U. PA. L. REV. 875 (1999). Firms may also contractually prohibit parallel trade of their products.

60. Case C-306/96, Javico Int'l v. Yves Saint Laurent Parfums SA, 1998 E.C.R. I-1983, [1998] 5 C.M.L.R. 172 (1998).

61. BERNDT, *supra* note 44, at 8-10; PHILIPS, *supra* note 43, at 27.

62. Aspirin might be considered a fungible commodity. The active ingredient is well known and unprotected by patents. Yet, the aspirin market is filled with differentiated

between similar products from competing companies, but parallel traders force companies to confront movements of differentially priced products between geographic markets. Trademarks and laws constraining parallel trade support product differentiation. Granting patents for modest variations in dosage and formulations also supports product differentiation.

Laws regulating pharmaceutical marketing also affect the potential for arbitrage. Drug companies target both consumers and physicians[63] with their marketing efforts: Overall, U.S. promotional spending on prescription drugs in 2000 totaled $15.7 billion.[64] Even after generic entry, these marketing efforts are remarkably effective in retaining market share.[65] Finally, transaction costs also influence the ease of substitution. If laws raise arbitrage transaction costs, product differentiation is supported, and arbitrage is hindered.

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products. Some aspirins are marketed with brand names as proxies for safety and reliability. Others are compounded with other ingredients such as 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.

63. Companies spend billions of dollars to employ product representatives, who meet with doctors in various venues. In 2000, the industry employed 83,000 drug representatives at a cost of $4 billion. NAT'L INST. FOR HEALTH CARE MGMT. RESEARCH & EDUC. FOUND., PRESCRIPTION DRUGS AND MASS MEDIA ADVERTISING 5 (2001) [hereinafter NIHCM]. Free samples valued at $7.9 billion were given to doctors in 2000, and $1.9 billion was spent on educational conferences for doctors. *Id.* These efforts encourage particular prescribing habits and shift demand between drugs through substitution. *Id.* at 7; *see also* SCHNEIDER, *supra* note 4, at 26-36 (fraud cases); Compliance Program Guidance for Pharmaceutical Manufacturers, 68 Fed. Reg. 3,731, 23,735-38 (May 5, 2003). The industry has also taken steps to suppress negative research. *See* Angell, *supra* note 6, at 62; NAT'L INSTS. OF HEALTH, REPORT OF THE NATIONAL INSTITUTES OF HEALTH BLUE RIBBON PANEL ON CONFLICT OF INTEREST POLICIES 1-5 (2004), http://www.nih.gov/about/ethics_COI_panelreport.pdf [hereinafter NIH, CONFLICT OF INTEREST].

64. NIHCM, *supra* note 63, at 4. 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 4. In 2000, U.S. unit sales of the fifty most heavily advertised drugs rose at six times the rate of other drugs. *Id.* at 7.

65. CONG. BUDGET OFFICE, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY, at xii-xiii (1998) [hereinafter CBO, INCREASED COMPETITION].

3. Government Regulation of Pharmaceuticals

Pharmaceutical regulation influences substitution, transaction costs, and arbitrage. Two major legal categories are particularly relevant to pharmaceutical arbitrage: IP laws and national drug regulatory agencies (NDRAs).

i. Intellectual Property (IP) Laws

IP laws facilitate pharmaceutical differential pricing by creating legally enforceable rights, which in turn support the appropriation of rents. Pharmaceutical patents prevent substitution by identical compounds during the patent period. Trademarks support brand identification and differentiation of products to consumers, hindering consumer confusion or unintended substitution.[66]

In many countries, the first sale of a patented product exhausts the public law rights of the patent holder for that item.[67] This exhaustion rule is a necessary condition[68] to legal domestic arbitrage, as it permits domestic resale by the purchaser without the permission of the patent holder.[69] 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

66. 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).

67. ROTHNIE, *supra* note 66, at 125-42 (Anglo-Commonwealth patent law); *id.* at 143-50 (U.S. patent law).

68. It is necessary, but not sufficient: Significant price differentials and relatively low transaction costs 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 66, at 477, 494-97. *See generally* DG TRADE, *supra* note 42, § 3.

69. Domestic parallel trade in pharmaceuticals is legal within the EU and the United States. *See, e.g.*, Case 187/80, Merck v. Stephar, 1981 E.C.R. 2063, [1981] 3 C.M.L.R. 463 (holding that parallel drug trade is legal in the EU); DONALD S. CHISUM, CHISUM ON PATENTS § 16.03[2] (2003) (explaining the U.S. domestic exhaustion rule). *But see* Case T-41/96, Bayer A.G. v. E.C. Commission, [2001] 4 C.M.L.R. 4 (holding that unilateral acts by pharmaceutical company to choke off supply of drugs to parallel exporters is not actionable under EU law); Glaxo Group Ltd. v. Dowelhurst Ltd. [2004] EWCA Civ. 129 (requiring repackaging in some cases to protect the trademark).

parallel trade.[70] United States law only recently rejected the international patent exhaustion rule,[71] and the extent of the rejection may not yet be clear,[72] although the recent Free Trade Agreement with Australia commits

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70. DG TRADE, *supra* note 42, § 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 1, art. 6. Some commentators writing on the economics of essential medicines mention in passing that U.S. patent law rejects the international exhaustion rule. *See, e.g.*, JOHN H. BARTON, DIFFERENTIATED PRICING OF PATENTED PRODUCTS (WHO, Comm'n on Macroeconomics & Health, Working Paper No. 2, 2001); JEAN O. LANJOUW, INTELLECTUAL PROPERTY AND THE AVAILABILITY OF PHARMACEUTICALS IN POOR COUNTRIES 19 n.29 (Ctr. for Global Dev., Working Paper No. 5, 2002), *reprinted in* 3 INNOVATION POLICY AND THE ECONOMY (2002) [hereinafter LANJOUW, INTELLECTUAL PROPERTY].

71. One distinguished commentator states, without discussion, that the 1994 amendments reject international exhaustion for U.S. patents, which might imply that the Uruguay Round required this result. CHISUM, *supra* note 69, § 16.05[3]. The amendment was included as part of the Uruguay Round Agreements Act by which the United States joined the WTO. Uruguay Round Agreements Act, Pub. L. No. 103-465, 108 Stat. 4809 (1994). Section 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 United States 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. 103-826(I), at 8 (1994). 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." Cong. Research Serv., Bill Summary & Status, H.R. 5110 (Pub. L. No. 103-465), 103d Cong. (Sept. 27, 1994).

72. Four points are important. First, prior to the 1994 amendments, U.S. patent law was leaning in favor of the international exhaustion rule, a trend which resulted in the 1995 U.S. Supreme Court case, *K Mart Corp. v. Cartier, Inc.*, 486 U.S. 281 (1988). *See also* CHISUM, *supra* note 69, § 1605[3]; ROTHNIE, *supra* note 66, at 183. 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 69, § 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. Finally, the heuristic of optimality, *see infra* Section I.D, suggests that any provision which strengthens drug patent rights will enhance beneficial innovation only if rents are sub-optimal. This issue was not demonstrated to Congress in the legislative history to the 1994 amendment.

both parties to the domestic exhaustion rule.[73]

If the United States does follow the domestic exhaustion rule for pharmaceutical patents, drugs sold in the United States, exported to Canada, and then re-imported back into the United States arguably qualify for domestic exhaustion.[74] However, the Prescription Drug Marketing Act of 1987 blocks reimportation by anyone other than the manufacturer, forbidding this form of arbitrage.[75]

ii. National Drug Regulatory Agencies

The TRIPS Agreement generally leaves the drug approval process to individual countries.[76] The global diversity of regulatory actors creates the possibility that each country will have a unique drug regulatory environment, with different approaches to issues such as generic substitution, drug approval, reimbursement, parallel trade, advertising, and pharmaceutical arbitrage. In addition, each country's market may differ due to other significant factors such as economic development and demand elasticity. The net result is that law assists in the creation of unique market characteristics in each country, which may result in differentiated prices either by facilitating voluntary differentiation and impeding conditions necessary for arbitrage, or by taking actions, such as price controls, that essentially demand a differentiated scheme.

To begin, a country's regulatory conditions may uniquely affect the potential for product differentiation—an impediment to arbitrage—by allowing or disallowing certain marketing efforts or dictating transactions costs. For example, in 1997, the United States's national drug regulatory

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73. In 2004, the U.S.-Australia Free Trade Agreement committed both parties to the domestic exhaustion rule for patents. Free Trade Agreement, May 18, 2004, U.S.-Austl. § 17.9.4, http://www.ustr.gov/Trade_Agreements/Bilateral/Australia_FTA/Final_Text/Section_Index.html.

74. *See* Rebecca S. Eisenberg, *The Shifting Functional Balance of Patents and Drug Regulation*, 19 HEALTH AFF. 119, 129-32 (2001). Re-imported patented drugs are produced in the United States under proper authority, legally exported to a second country (such as Canada) and then re-imported by a third party, arguably exhausting U.S. 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 supra* notes 71-72. As discussed *infra* Section II.B, Canadian pharmaceutical arbitrage has recently exploded despite this restriction.

75. Prescription Drug Marketing Act of 1987, 21 U.S.C. §§ 331(t), 381(d) (2000).

76. TRIPS Agreement, *supra* note 1, art. 1, § 1.

agency, the Food and Drug Administration (FDA),[77] modified its regulations to permit direct to consumer (DTC) advertising for pharmaceutical drugs.[78] Virtually no other countries permit the practice.[79] The creation of the DTC rule by the FDA modifies information costs related to substitution.[80]

Other government regulations also influence pharmaceutical marketing. For example, federal law prohibits the sale of a drug sample[81] or the domestic resale of deeply-discounted drugs sold to certain hospitals,[82] hindering arbitrage of these products and thus supporting their provision at differential prices. The U.S. 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.[83]

Regulatory postures can alter manufacturing costs of potential competitors. The current de facto global standard for quality pharmaceutical manufacturing is the Standard of Good Manufacturing

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77. 21 U.S.C. § 355 (2000).

78. The regulations are now found at 21 C.F.R. § 202.1 (2004).

79. In recent years, only the United States and New Zealand permit DTC broadcast ads. NIHCM, *supra* note 63, at 16. In 2002, Canada permitted restricted DTC advertising and is affected by spillover from American media. CAN. INST. FOR HEALTH INFO., DRUG EXPENDITURE IN CANADA: 1985-2002, at 41 (2003). In the 2004 U.S.-Australia Free Trade Agreement, web-based DTC advertising is permitted. Free Trade Agreement, *supra* note 73, Annex 2-C, ¶ 5.

80. PHILIPS, *supra* note 43, ch. 12. DTC campaigns build consumer demand, encouraging the patient to ask for a prescription by name. Advertising shifts the demand curve for prescription drugs to the right. NIHCM, *supra* note 63, at 2 (noting that DTC advertising increases consumer sales of patented pharmaceuticals); CBO, INCREASED COMPETITION, *supra* note 65, at 20. 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%. Stephen Heffler et al., *Health Spending Projections for 2002-2012*, HEALTH AFF., Feb. 7, 2003 (Web Exclusive), *at* http://content.healthaffairs.org/cgi/content/full/hlthaff.w3.54v1/DC1. 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 AFF. 210, 213 (2001). In 2000, the most heavily advertised drugs accounted for 47.8% of the $20.8 billion increase in U.S. retail spending on prescription drugs. NIHCM, *supra* note 63, at 2.

81. 21 U.S.C. §§ 331(t), 353(d) (2000).

82. *Id.* § 353(c)(3).

83. SCHNEIDER, *supra* note 4, at 26-36 (reviewing False Claim Act litigation against drug companies, particularly involving marketing related fraud); Compliance Program Guidance for Pharmaceutical Manufacturers, 68 Fed. Reg. 23,731, 23,733-39 (May 5, 2003).

Practice (GMP). PhRMA companies are now cooperating with the United States, the EU, and Japan to develop a higher global standard, known as the International Conference on Harmonization (ICH).[84] Imposition of ICH would discourage substitution of drugs manufactured by less-expensive non-OECD[85] pharmaceutical companies. This effort could be viewed as rent-seeking behavior through technical standards. Likewise, donor agencies often face substitution choices during the procurement process, which may be subject to regulation or political intervention.[86]

Furthermore, international arbitrage may simply be proscribed by NDRAs. Under the Food, Drug and Cosmetics Act, drugs cannot be imported unless approved by the FDA,[87] creating a non-tariff barrier to international trade. Some drugs are produced in the United States and exported to countries with price controls such as Canada.[88] Since the drugs are produced in the United States, they arguably comply with FDA rules, and could be re-imported back into the United States by arbitrageurs. However, the U.S. Prescription Drug Marketing Act of 1987 prohibits the reimportation of a prescription drug by anyone other than the manufacturer.[89] The law was ostensibly intended to address safety concerns for the U.S. pharmaceutical supply chain,[90] but its effect is to prevent

84. GRAHAM DUKES, UN MILLENNIUM PROJECT, INTERIM REPORT OF TASK FORCE 5 WORKING GROUP ON ACCESS TO ESSENTIAL MEDICINES 32 (2004).

85. The OECD is the Organisation for Economic Co-operation and Development; its membership consists almost exclusively of high income countries. *See* OECD, Information by Country, *at* http://www.oecd.org/infobycountry/0,2646,en_2649_201185_1_1_1_2_1,00.html; World Bank, Data & Statistics: Country Group, *at* http://www.worldbank.org/data/countryclass/classgroups.htm (last visited Nov. 22, 2004). Non-OECD pharmaceutical companies are essentially those based outside of Japan, North America, and Europe, such as India's Cipla and Ranbaxy. These companies are typically best known for their production of generic products. *See, e.g.*, Donald G. McNeil, Jr., *Selling Cheap 'Generic' Drugs, India's Copycats Irk Industry*, N.Y. Times, Dec. 1, 2000, at A1.

86. The United States's unilateral effort on AIDS (PEPFAR) has chosen to ignore the WHO prequalification process, as well as all recipient country drug regulatory agencies, and now imposes a supplementary FDA approval process for AIDS drug procurement. Sarah Lueck, *White House Aims To Answer Critics of Its AIDS Fight*, WALL ST. J., Apr. 29, 2004, at A9; Sarah Lueck, *White House Gets Pressure on AIDS Plan*, WALL ST. J., Mar. 25, 2004, at A4. This decision, ostensibly made on quality grounds, also supports the product line of PhRMA companies by imposing additional regulatory requirements on their generic competitors located in India, South Africa, Thailand, and Brazil.

87. 21 U.S.C. §§ 360(i), 381(a) (2000).

88. *See infra* Subsection II.A.2.

89. 21 U.S.C. §§ 331(t), 381(d) (2000).

90. H.R. REP. No. 100-76, at 7 (1987).

international pharmaceutical arbitrage or parallel trade.[91]

Finally, PhRMA companies generally do not enjoy unconstrained monopoly power to set prices on patented drugs. In high income countries, regulatory systems, as well as payor monopsony, will likely yield countervailing pricing power. In some countries, the government sets pharmaceutical prices by regulatory process, including reference pricing[92] and rate setting.[93] In others, price regulation occurs when the government enters the market as a purchaser and acts with monopsony power.[94] Private payors (health plans or their agents such as pharmacy benefit managers) may either mimic the government prices, or utilize their own market power to negotiate prices.[95] Moreover, most third-party payors have pharmaceutical 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. In the United States, state and federal laws generally support these efforts.[96]

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91. The government also has the power to seize counterfeit or improperly diverted drugs. For an interesting story on the diversion of Serostim within the United States, see Christopher Windham, *Cracking Down on Illicit Use of AIDS Drugs*, WALL ST. J., Jan. 19, 2004, at B1.

92. PATRICIA DANZON & JOHATHAN D. KETCHAM, REFERENCE PRICING OF PHARMACEUTICALS FOR MEDICARE: EVIDENCE FROM GERMANY, THE NETHERLANDS AND NEW ZEALAND (Nat'l Bureau of Econ. Research, Working Paper No. W10007, 2003) (discussing reference price systems in Germany, The Netherlands, and New Zealand).

93. House of Commons Select Comm. on Health, Minutes of Evidence (Jan. 23, 2002), http://www.publications.parliament.uk/pa/cm200102/cmselect/cmhealth/515/2012321.htm (examination of Dr. John Patterson, President-elect, Association of the British Pharmaceutical Industry) ("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 United States effectively sets rates for government purchase of services from physicians and hospitals, but generally not for pharmaceuticals.

94. In the United States, 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 (to be codified at 42 U.S.C. § 1395).

95. CBO, INCREASED COMPETITION, *supra* note 65, at xi.

96. *See, e.g.*, W. VA. CODE § 30-5-12 (2004) (allowing pharmacists to substitute generic medicines for brand name medicines without approval from the prescriber); *id.* § 23-4-3 (requiring generic substitution within the Workers' Compensation program). *But see* DANZON & KETCHAM, *supra* note 92, at 7 (noting that Germany restricts generic substitution).

iii. The Hatch-Waxman Act

Traditionally, IP law regulates the economic incentives of innovation while NDRA regulations and related laws control drug efficacy and safety. However, the patent system is not the only source of exclusive, or monopoly, rights. Under the Hatch-Waxman Act[97] and other legislation such as the Orphan Drug Act,[98] the FDA may grant additional exclusive marketing periods under an array of circumstances—for example, rewarding first-mover generic drugs,[99] certain drugs for uncommon conditions (so-called orphan drugs),[100] or compliance with social goals such as testing drugs for efficacy and safety on children.[101] Indeed, when examining the incentives for pharmaceutical innovation, it is not the length of the patent period that matters most but the duration of this exclusive marketing period.[102] PhRMA companies are maximizing their opportunities under these provisions.[103]

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97. 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]. 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, 156 (2000).

98. 21 U.S.C. §§ 360aa-360ee (2000).

99. *Id.* § 355(j).

100. *Id.* §§ 360aa-360ee.

101. *Id.* § 355a.

102. The term "exclusive marketing period" means the actual period during which a pharmaceutical company sells an 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, the use of litigation and agreements to forestall competitive entry, and the evergreening of patents through filings for new uses and formulations.

103. For example, the number of putative orphan drugs qualifying for tax credits and extended exclusive marketing periods has 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. U. L.Q. 691, 692, 704-06 (1993) (noting that the FDA designated AZT as an orphan drug in 1987 and half of AIDS drugs as of August 1991 were designated as orphans); John J. Flynn, *The Orphan Drug Act: An Unconstitutional Exercise of the Patent Power*, 1992 UTAH L. REV. 389 (noting that the 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 now $200 million per year, not including the cost of the grant of market exclusivity. JOINT COMM. ON TAXATION, ESTIMATES OF FEDERAL TAX EXPENDITURES FOR FYS 2004-2008 (Joint Committee Print 2003). Public Citizen notes the

The 1984 Hatch-Waxman Act was the first major piece of legislation to link patent law and FDA regulations in this way. The Act regulates patent expiry and generic entry following patent expiration, directly addressing the balance between innovation and access.[104] The United States is now exporting portions of the Hatch-Waxman Act to other countries through bilateral free trade agreements.[105]

After a patent or exclusive marketing period expires,[106] 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. PhRMA companies have resorted to strategic litigation and collusive agreements to lengthen effective exclusive marketing periods.[107] These abuses prompted amendments to Hatch-Waxman in 2003.[108] PhRMA companies are already responding with new tactics to keep generic drugs off the market by denying the generic companies an adequate financial return for the expensive generic approval process.[109]

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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 huge financial rewards exceeding $1 billion. PUBLIC CITIZEN'S CONG. WATCH, PUBLIC CITIZEN, THE OTHER DRUG WAR II: DRUG COMPANIES USE AN ARMY OF 623 LOBBYISTS TO KEEP PROFITS UP 4 (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 five year AIDS program. FDA, THE PEDIATRIC EXCLUSIVITY PROVISION: STATUS REPORT TO CONGRESS (2001).

104. *See, e.g.*, Elizabeth Stotland Weiswasser & Scott D. Danzis, *The Hatch-Waxman Act: History, Structure, and Legacy*, 71 ANTITRUST 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 30, at 12 (emphasis in original).

105. *See, e.g.*, Free Trade Agreement, *supra* note 73, §17.9.6.

106. By the late 1990s, the U.S. pharmaceutical exclusive marketing period was approximately fourteen years. CBO, INCREASED COMPETITION, *supra* note 65, at 45-48. If someone undertakes to update this figure, care should be taken to account for all of the factors affecting effective exclusive rights.

107. FTC, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION 13-23 (2002).

108. Pub. L. No. 108-173, 117 Stat. 2066 (2003), tit. IX (codified at 21 U.S.C. § 355(j) and uncodified). The Congressional Research Service prepared a summary of the Act which provides some guidance on Congress's intent in amending Hatch-Waxman. *See* Cong. Research Serv., Prescription Drug and Medicare Improvement Act of 2003, Bill Summary and Status, S.1, 108th Cong. (June 13, 2003).

109. Leila Abboud, *Drug Makers Use New Tactic To Ding Generics*, WALL ST. J., Jan. 27, 2004, at B1.

D. The Heuristic of Globally Optimal Pharmaceutical Rents[110]

1. Nonrival Access to Pharmaceutical Knowledge

The goal of IP laws should be to maximize nonrival access to pharmaceutical knowledge, with just enough legal support for the appropriation of rents to protect socially optimal R&D. Since pharmaceutical knowledge is nonrival, it should be disseminated in the widest possible fashion at the lowest possible cost for the greatest possible benefit to global public health. This Article describes this condition as "nonrival access."

The pharmaceutical industry has borrowed language from the world of physical property to attack nonrival access. They call nonrival access "theft" or "piracy." At best, nonrival users are characterized as "free riders."[111] These terms are inappropriate since nonrival use of pharmaceutical knowledge does not cause anything to be lost,[112] so long as the socially optimal level of appropriation for R&D is still achieved. In a world of excessive rents, we should call it theft (or, in some cases, genocide) to deny nonrival access to low income populations.

For the pharmaceutical industry, the globally optimal level of appropriation through rents[113] must be sufficient to fund the socially

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110. Once again, the broader term *rents* is used here in lieu of *patent rents* in order to encompass the various mechanisms beyond patent law which facilitate appropriation, as described *supra* Section I.C. The use of the term *patent rents* is meant to signify only the narrow meaning of patent-based appropriation.

111. DRAHOS WITH BRAITHWAITE, *supra* note 2, at 19-29 (piracy); LEMLEY, *supra* note 20, at 3-16 (property and free riding); STERK, *supra* note 20, at 24-25 (analogies to tangible property).

112. *Cf.* Selling Life-Saving Drugs to Poorer Countries: At What Cost?, Research at Penn (Nov. 6, 2002), *at* http://www.upenn.edu/researchatpenn/article.php?504&hlt.

113. The economic analysis of socially optimal patents has been undertaken by Nordhaus and Scherer. NORDHAUS, INVENTION, GROWTH & WELFARE, *supra* note 36, at 70-92; Nordhaus, *The Optimum Life of a Patent*, *supra* note 36, at 428; Scherer, *Optimal Patent Life*, *supra* note 36, at 422. 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* note 36, 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* note 36, 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

optimal level of R&D. Optimization must balance concerns of cost, quality, and access, looking for the greatest net gain to global public welfare. Excessive rents harm human health without advancing socially optimal R&D. Society must decide when the best level of appropriation has been reached.[114]

Maximizing R&D at all costs should not be our objective. Resources devoted to R&D are not available for other uses.[115] Uwe Reinhardt puts it this way: "Year after year, the last dollar spent on drug research and development (R&D) should yield society as much benefit as it would have yielded if it had been spent to produce other goods or services."[116]

We should also avoid the assumption that all R&D targets are equally valuable. Some innovations are more valuable than others. Companies allocate research funds in response to price signals from commercial pharmaceutical markets. As a result, Americans now have a third drug for erectile dysfunction,[117] and funds for neglected disease innovation are literally going to the dogs,[118] but malaria and AIDS vaccines are not

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problem ex-ante." PHILIPSON & MECHOULAN, *supra* note 30, at 12, 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).

114. 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 & MECHOULAN, *supra* note 30, at 2.

115. Currently the United States spends more than fifteen percent of its GDP on health care. Robert Pear, *Health Spending Rises to Record 15% of Economy*, N.Y. TIMES, Jan. 9, 2004, at A16. Perhaps we can agree that increasing pharmaceutical R&D to twenty percent or fifty percent of GDP would be excessive.

116. Uwe E. Reinhardt, *An Information Infrastructure for the Pharmaceutical Market*, 23 HEALTH AFF. 107 (2004).

117. Viagra (sildenafil) was approved by the FDA in 1998. *First Oral Therapy for Erectile Dysfunction*, 28 FDA MEDICAL BULL. 1 (1998), http://www.fda.gov/medbull/summer98/erectile.html. Levitra (vardenafil) was approved in August 2003. FDA, Talk Paper, FDA Approves New Drug for Treatment of Erectile Dysfunction in Men (Aug. 19, 2003), http://www.fda.gov/bbs/topics/ANSWERS/2003/ANS01249.html. Cialis (tadalafil) was approved in November 2003. FDA, Talk Paper, FDA Approves Third Drug To Treat Erectile Dysfunction (Nov. 21, 2003), http://www.fda.gov/bbs/topics/ANSWERS/2003/ANS01265.html.

118. 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

available.[119]

You get the sense that ships are passing in the night on this issue. James Love estimates the static global deadweight loss on pharmaceutical patents at over $400 billion per year,[120] and Larry Lessig implores us not to allow IP law to be perverted while a holocaust devastates millions in the developing world.[121] Meanwhile Joseph DiMasi and Henry Grabowski suggest that the "dynamic benefits created by patents on pharmaceuticals can, and almost surely do, swamp in significance their short-run inefficiencies."[122] Yet, in a major study, the Congressional Budget Office conceded that no one knows whether current levels of pharmaceutical R&D are optimal.[123] This is the pressing question.

2. Globally Sub-Optimal Pharmaceutical Rents

Globally sub-optimal pharmaceutical rents would stifle the production of pharmaceutical knowledge, creating a generational equity issue. The present group of patients might benefit from sub-optimal pharmaceutical rents because such rents result in innovative treatments that are cheaper and thus more accessible, but future quality would be compromised. Pharmaceutical companies would invest less when creating inappropriable knowledge. This is the nightmare scenario portrayed by PhRMA companies when they argue that constraints on their ability to appropriate rents will squelch innovation.

Behavioral Drugs for Dogs (Jan. 5, 1999), http://www.fda.gov/bbs/topics/answers/ans00934.html. Perhaps soon a drug will be developed for erectile dysfunction in dogs.

119. For an introduction to donor efforts led by the Bill & Melinda Gates Foundation to stimulate development of a malaria vaccine, see Malaria Vaccine Initiative, *at* http://www.malariavaccine.org.

120. James Love, *supra* note 33, at 2.

121. Lawrence Lessig, *The International Information Society*, 24 LOY. L.A. ENT. L. REV. 33, 36-37 (2004).

122. JOSEPH A. DIMASI & HENRY G. GRABOWSKI, PATENTS AND R&D INCENTIVES: COMMENTS ON THE HUBBARD AND LOVE TRADE FRAMEWORK FOR FINANCING PHARMACEUTICAL R&D 2 (2004) (citation omitted), http://www.who.int/intellectualproperty/news/en/Submission3.pdf. DiMasi and Grabowski cite the 2003 study by Philipson and Mechoulan, but that study assumes sub-optimality rather than proves it. *See* PHILIPSON & MECHOULAN, *supra* note 30.

123. 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 65, at 48.

3. Globally Supra-Optimal Pharmaceutical Rents

Globally supra-optimal pharmaceutical rents are rarely recognized as a potential problem by PhRMA companies. By definition, supra-optimal pharmaceutical rents are not necessary to fund R&D; they simply harm consumers by raising prices and restricting access without providing the counterbalancing benefits of future innovation.

i. Are Supra-Optimal Pharmaceutical Rents Possible?

One economist reviewer of an earlier draft of this Article suggested that pharmaceutical rents cannot be supra-optimal because PhRMA companies have not fully appropriated all consumer surplus associated with their products.[124] This is another way of saying that PhRMA companies have not yet achieved first-degree differential pricing (or Ramsey Optimal Pricing). While Ramsey Optimal Pricing would maximize the sales and profits of PhRMA companies, it does not respond to the distributional balance between innovation and access. Nor does it address the quality of research undertaken with the surplus so completely extracted from consumers. In a market beset with profound agency problems and information disparities, it is absurd to assume that consumers will purchase pharmaceuticals at the cost-effective price. Given what we know about pharmaceutical markets, it is at least equally likely that PhRMA companies will stimulate demand which varies from optimal therapeutic need, while neglecting less lucrative markets.

This critique also fails to account for important negative externalities. PhRMA companies have failed to get the right pills to the right people at the right price. If another regime would result in greater global welfare (improved therapeutic outcomes) without damage to dynamic innovation incentives, then it should be preferred even if it reduces pharmaceutical rents slightly.

Consider the vast global gains in welfare which would result if nonrival access could be accomplished without diminishing the incentive to innovate. The opportunity cost of failing to do so is staggering. The net gains to global social welfare would be very significant, even if nonrival access came at the cost of a modest slice of innovation. It is in this sense that pharmaceutical rents may be supra-optimal.

124. I thank Aidan Hollis for this comment. My criticisms are not directed at him.

ii. Are Pharmaceutical Rents Supra-Optimal?

Some empirical evidence suggests that PhRMA companies earn well above market rates of return, one possible indicator of supra-optimal pharmaceutical rents.[125] The industry's long-term profits are four times the rate of the Fortune 500.[126] 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.[127]

Calculating optimal pharmaceutical rents must account for other sources of public funding for R&D, such as government grants, direct government expenditures, foundation donors, and tax incentives. The industry receives substantial tax incentives, resulting in an effective U.S. federal income tax rate of 16.2%, compared with 27.3% generally.[128]

The ways in which PhRMA companies currently opt to expend their cash flows may also indicate supra-optimality. The pharmaceutical industry currently spends more on sales and marketing than on R&D.[129] Large marketing expenses are not proof that pharmaceutical rents are supra-optimal, but merely indicate that the industry believes the return on investment in marketing is greater than alternative investments such as R&D. If the industry holds a relatively low view of the value of an additional

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125. 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 PhRMA company data rather than a truly objective data set. DiMasi et al., *supra* note 29. IRS data shows extraordinary profits and low taxation but is protected against public disclosure by the Internal Revenue Code. *See* GARY GUENTHER, CONG. RESEARCH SERV., FEDERAL TAXATION OF THE DRUG INDUSTRY FROM 1990 TO 1996 (1999). Accurate pricing data is unavailable outside of the companies. CBO, INCREASED COMPETITION, *supra* note 65, at 20. On the theoretical front, useful questions are posed by Reinhardt, *supra* note 116; and William S. Comanor, *Political Economy of the Pharmaceutical Industry*, 24 J. ECON. LIT. 1178, 1182-86 (1986).

126. DAVID H. KRELING ET AL., THE KAISER FAMILY FOUND., PRESCRIPTION DRUG TRENDS: A CHARTBOOK UPDATE exhibit 32 (2001). The judgment of the equity markets is significant, even under a weak form of the efficient capital markets hypothesis.

127. GUENTHER, *supra* note 125.

128. *Id.*

129. KRELING ET AL., *supra* note 126, exhibit 30 (noting that the top ten major pharmaceutical manufactures in 2000 spent 34.4% of their revenues on "marketing, general and administrative" expenses and 13.7% on "research and development."). *But see* Uwe E. Reinhardt, *Perspectives on the Pharmaceutical Industry*, 20 HEALTH AFF. 136 (2001) (suggesting that 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.

dollar of R&D investment, then perhaps society would be better served with that additional dollar being used to provide life-saving access to medicines.

Some scholars, including proponents of the anti-commons movement,[130] suggest that the neo-classical link between patents and innovation is overstated, particularly for industries marked by cumulative innovation[131] such as genetics.[132] If so, optimal rents may be lower than previously expected.

The most important data required to resolve this question are in the hands of the pharmaceutical industry and are not available in a reliable form to independent researchers.[133] This fact alone is a compelling reason to demand transparency. It certainly seems plausible to presume that supra-optimal rents are currently being collected. The burden of coming forward with contrary evidence should be placed on the parties controlling the relevant information: the PhRMA companies.

4. Implications of Global Optimality

Pending the resolution of the empirical issue, the concept of globally optimal pharmaceutical rents is useful as a heuristic tool. The following Subsections outline several implications which follow from applying this tool to pharmaceutical markets.

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130. The leading article is Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research,* 280 SCIENCE 698 (1998). For a recent study on the importance of maintaining a scientific commons, see J.H. Reichman & Paul F. Uhlir, *A Contractually Reconstructed Research Commons for Scientific Data in a Highly Protectionist Intellectual Property Environment,* 66 LAW & CONTEMP. PROBS. 315 (2003).

131. 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 PhRMA companies are eager to publish and forego patents, it is a nascent trend.

132. The work of Tim Hubbard and James Love is particularly interesting in this regard. Hubbard & Love, *supra* note 27.

133. *See supra* note 125. Pharmaceutical pricing and profitability data are notoriously opaque and misleading. SCHNEIDER, *supra* note 4; Gardiner Harris, *Drug Companies Settle 7 Suits for $1.6 Billion,* N.Y. TIMES, Nov. 6, 2003, at 8 ("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. DANZON & TOWSE, *supra* note 12, at 16-20. I suggest that transparency will better serve global public health.

i. Nonrival Access to Pharmaceutical Innovation

Patented pharmaceuticals can be delivered at marginal cost of production to low income populations without harming innovation. The majority of AIDS patients in low income countries are quite poor and are not part of the global market for patented drugs. Supplying their needs is a humanitarian response, and pharmaceutical companies do not actually lose viable commercial markets as a result.[134] These non-market patients could receive unlicensed or royalty-free drugs without impacting the cash flow of PhRMA companies.[135]

Even if global pharmaceutical rents are currently sub-optimal, unlicensed or royalty-free production should still be allowed so long as it does not replace any commercial market, and thus does no financial harm to the patent owner.[136] Certainly if global pharmaceutical rents are now supra-optimal, PhRMA 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 markets, even with some displacement of commercial markets. The magnitude of expense and market loss that could be tolerated would depend on the amount by which pharmaceutical rents are supra-optimal.

a. The Need for a Credible Threat of Compulsory Licensing

OECD members with monopsonistic public sector purchasing of pharmaceuticals can negotiate or impose domestic second-degree differential pricing to meet local needs. For developing countries, which often lack a significant publicly financed pharmaceutical sector,

134. *See* John H. Barton, *TRIPS and the Global Pharmaceutical Market*, 23 HEALTH AFF. 146, 148 (2004).

135. Frederic M. Scherer recently made a similar point when he argued for allowing free riding by developing countries on pharmaceutical patents. F.M. Scherer, *A Note on Global Welfare in Pharmaceutical Patenting*, 27 WORLD ECON. 1127, 1141 (2004) [hereinafter Scherer, *Global Welfare*].

136. Philipson and Mechoulan criticize this position, but their stance is undermined if global pharmaceutical rents are supra-optimal. PHILIPSON & MECHOULAN, *supra* note 30, 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.

compulsory licensing, or at least the credible threat thereof, may be required.

At the Fourth WTO Ministerial Conference in Doha, WTO members agreed to the Doha Declaration as an interpretation of TRIPS.[137] The Doha Declaration allows WTO Members to take measures to "protect public health and, in particular, to promote access to medicines for all."[138] Specifically, WTO Members may compel licensure to protect public health, without limitation to AIDS or any particular disease.[139]

Sovereign threats of such compulsory licenses, public pressure from NGOs, and actual competition from generic[140] companies persuaded PhRMA companies and the United States to embrace differential pricing of antiretroviral (ARV) medications for a number of poor countries combating HIV/AIDS. Médecins sans Frontières (MSF) and others consider the threat and use of compulsory licenses to have been essential in convincing companies to establish meaningful differential pricing

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137. *Doha Declaration on TRIPS*, *supra* note 32. 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 in CARLOS M. CORREA, IMPLICATIONS OF THE DOHA DECLARATION ON THE TRIPS AGREEMENT AND PUBLIC HEALTH 5 (WHO, Health Econ. and Drugs, EDM Series No. 12, 2002), http://www.iprsonline.org/resources/health.htm [hereinafter CORREA, IMPLICATIONS OF DOHA]. The legal status of the Cancun General Council Decision is a joint commitment by WTO Members to abide by its terms in good faith. Press Release, European Comm'n, 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 General Council Decision.) Practically speaking, it would be virtually impossible to prevail at DSB on a provision contrary to the Cancun General Council Decision. The legal status of both Doha and Cancun are expected to be clarified in a planned 2004 amendment to TRIPS. General Council, World Trade Org., *Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health: Decision of the General Council*, WT/L/540, ¶ 11 (Aug. 30, 2003) [hereinafter *Cancun General Council Decision*]; *see also Doha Declaration on TRIPS*, *supra* note 32, ¶ 7.

138. TRIPS Agreement, *supra* note 1, art. 31(f); *Doha Declaration on TRIPS*, *supra* note 32, ¶ 4.

139. *Doha Declaration on TRIPS*, *supra* note 32, ¶ 5; 't Hoen, *supra* note 7, at 40-41.

140. This Article is generally focused on generics of controversial legal status, sometimes referred to as "unlicensed" generics (i.e., a copy of a patented pill made by a manufacturer that has not been authorized by the originator company). This terminology can be confusing in light of the role of compulsory licenses and the questionable need for licensing in some situations. It is simply important to keep in mind that we are not speaking simply of generics for off-patent products, but the more complex market for generics of drugs that may be subject to patents in the United States or elsewhere.

programs.[141] PhRMA companies strongly resisted both significant price reductions as well as generic ARV drugs, citing both TRIPS and domestic IP legislation.[142]

Several examples illustrate the effectiveness of the credible threat of generic production. Brazil's threat to issue a compulsory license, coupled with its non-recognition of pharmaceutical patents prior to the adoption of TRIPS, permitted the distribution of free ARVs within Brazil.[143] In January 2001, the United States requested a WTO panel against Brazil to prevent Brazilian "local manufacture" of ARVs.[144] Under international pressure, the United States withdrew the panel request on June 25, 2001, in the months leading up to the Fourth WTO Ministerial Conference in Doha.[145]

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141. MÉDECINS SANS FRONTIÈRES, SURMOUNTING CHALLENGES: PROCUREMENT OF ANTIRETROVIRAL MEDICINES IN LOW- AND MIDDLE-INCOME COUNTRIES 7, 9, 42 (2003), http://www.accessmed-msf.org/documents/procurementreport.pdf [hereinafter MSF, SURMOUNTING CHALLENGES] (report prepared by MSF at the request of the WHO); Marleen Boelaert et al., Letter to the Editor, 287 JAMA 840, 840 (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.").

142. MSF, SURMOUNTING CHALLENGES, *supra* note 141; Judy Rein, *International Governance Through Trade Agreements: Patent Protection for Essential Medicines*, 21 NW. J. INT'L L. & BUS. 379, 394-404 (2001); Susan K. Sell, *TRIPS and the Access to Medicines Campaign*, 20 WIS. INT'L L.J. 481, 491-96 (2002) [hereinafter Sell, *TRIPS*]; 't Hoen, *supra* note 7, at 30-33.

143. U.K. COMM'N ON INTELLECTUAL PROPERTY RIGHTS, INTEGRATING INTELLECTUAL PROPERTY RIGHTS AND DEVELOPMENT POLICY 43 (2002); JEROME H. REICHMAN WITH CATHERINE HASENZAHL, UNCTAD, NON-VOLUNTARY LICENSING OF PATENTED INVENTIONS: HISTORICAL PERSPECTIVE, LEGAL FRAMEWORK UNDER TRIPS, AND AN OVERVIEW OF THE PRACTICE IN CANADA AND THE USA 2 (Project on IPRs and Sustainable Development, Issue Paper No. 5, 2003); Jorge Bermudez, *Expanding Access to Essential Medicines in Brazil: Recent Economic Regulation, Policy-Making and Lessons Learnt*, *in* ECONOMICS OF ESSENTIAL MEDICINES, 178, 193 (2002).

144. Permanent Mission of the United States, *Brazil Measures Affecting Patent Protection, Request for the Establishment of a Panel by the United States*, WT/DS199/3 (Jan. 9, 2001), http://www.cptech.org/ip/health/c/brazil/Req4EstabPanel.html. 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 JOHN R. THOMAS, CONG. RESEARCH SERV., HIV/AIDS DRUGS, PATENTS AND THE TRIPS AGREEMENT: ISSUES AND OPTIONS 13-17 (2001) [hereinafter THOMAS, CRS REPORT].

145. CORREA, IMPLICATIONS OF DOHA, *supra* note 137, at 2 & n.6; THOMAS, CRS REPORT, *supra* note 144, at 15; 't Hoen, *supra* note 7, at 38-47.

Indeed, even the United States has resorted to this tactic in recent years: During the anthrax scare, threats of compulsory licensing of ciprofloxacin were instrumental in securing a lower price from Bayer,[146] and compulsory licensing remains an important remedy in litigation.[147]

Finally, voluntary no-royalty licenses, such as Merck's recent grant to South African-Indian company Thembalami Pharmaceuticals,[148] must be viewed in the context of South Africa's compulsory licensing law. That is, such licenses can be seen as responses to the looming threat of compulsory licensing.[149]

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146. Jill Carroll & Ron Winslow, *Bayer Agrees To Slash Prices for Cipro Drug*, WALL ST. J., Oct. 25, 2001, at A3 ("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 U.S. compulsory license statutes are 7 U.S.C. § 2404 (2000) (patents necessary for the nation's food supply); 17 U.S.C. § 115 (2000) (copyrights to certain musical works); 28 U.S.C. § 1498 (2000) (patents); 35 U.S.C. § 203 (2000) (patents developed through the use of government research funding under the Bayh-Dole Act); and 42 U.S.C. § 2183 (2000) (atomic energy). The U.S. compulsory license statutes do not contain the restrictions required by Article 31 of TRIPS. *See* TRIPS Agreement, *supra* note 1, art. 31. For an authoritative review of United States and Canadian experience with compulsory licensure, see REICHMAN WITH HASENZAHL, *supra* note 143, at 19-22.

147. Makan Delrahim, Deputy Assistant Attorney General, Antitrust Division, U.S. Department of Justice, 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).

148. Press Release, Merck & Co., Inc., Merck & Co., Inc. Grants License for HIV/AIDS Drug Efavirenz to South African Company, Thembalami Pharmaceuticals in Effort To Accelerate Access to Life-Saving Treatment (July 14, 2004), http://www.pressmethod.com/releasestorage/5003645.htm.

149. South Africa passed a compulsory licensing law in 1997, Medicines and Related Substances Control Amendment Act No. 90 of 1997 (Republic of South Africa). The government was promptly sued by PhRMA companies. The U.S. government suspended bilateral economic assistance to South Africa as punishment for defending the suit. Omnibus Consolidated and Emergency Supplemental Appropriations Act, 1999, Pub. L. No. 105-277, 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 U.S. trade pressure exerted upon South Africa. *See, e.g.*, 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 142, at 400-02; 't Hoen, *supra* note 7, at 30-31. Doha paragraph 4 discourages Members from exerting bilateral pressure which hinders the exercise of TRIPS and Doha rights. CORREA, IMPLICATIONS OF DOHA, *supra* note 137, at 12. The U.S. government and PhRMA companies relented under great pressure in April 2001,

Although threats of compulsory licensing may lead to differential pricing, it is worth noting that reliance on voluntary price discrimination to achieve marginal-cost distribution to low income populations has proven very disappointing. Over the past five years there have been many announcements of dramatic price cuts or voluntary programs, yet these announcements have not resulted in much actual treatment in 2004.[150] Each PhRMA company creates idiosyncratic policies specifying which countries qualify for differential pricing on any particular drug. 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. Transaction costs are high when essential access discounts are negotiated on a case-by-case basis. Company policies vary by the status of the purchaser (e.g., NGO, IGO, government, private buyer).

Voluntary programs of differential pricing also fail to achieve differential pricing at the marginal cost of production, which is absolutely necessary for nonrival access. Voluntary negotiations kept ARV prices unnecessarily high for years and delayed effective treatment for millions of dying people. The Médecins sans Frontières pricing guide confirms that most voluntary differential pricing programs continue to price significantly above generic levels,[151] a practice generally followed in the United States

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shortly before Doha. Editorial, *South Africa's Moral Victory*, 357 THE LANCET 1303 (2001); THOMAS, CRS REPORT, *supra* note 144, at 16.

150. See, for example, the correspondence concerning access to Pfizer's Diflucan Donation Program, announced with great fanfare several years ago, but apparently still unavailable on the ground in the Dominican Republic. E-mail from Eugene Schiff, Agua Buena, to Joseph Saba, Axios (Sept. 20, 2004) (on file with author). A five company group negotiated with five UN agencies for a year in 2000 and 2001 without tangible success. Each company ended up negotiating access deals with each individual country. Paul Blustein & Barton Gellman, *HIV Drug Prices Cut for Poorer Countries; Other Firms May Follow Merck's Lead*, WASH. POST, Mar. 8, 2001, at A1.

151. MÉDECINS SANS FRONTIÈRES, UNTANGLING THE WEB OF PRICE REDUCTIONS: A PRICING GUIDE FOR THE PURCHASE OF ARVS FOR DEVELOPING COUNTRIES (6th ed. 2004), http://www.accessmed-msf.org [hereinafter MSF, UNTANGLING THE WEB]. Merck makes Stocrin (efavirenz, EFV) 600 mg available in Columbia for US$767 per year. *Id.* at 9. The lowest cost generic provider is Hetero of India at US$347 per year. *Id.* at 12, 22. Merck matches the generic price only in Low Human Development Index (HDI) countries and Medium HDI countries with adult HIV prevalence of one percent or greater. *Id.* at 12. The distinction is lost on very poor persons living with HIV/AIDS in a Medium HDI country with prevalence under one percent, such as Columbia.

after generic market entry.[152]

Voluntary differential pricing should be extended to target populations in a larger group of countries. If pharmaceutical rents are supra-optimal, loss of some elite markets will not harm innovation. Even if pharmaceutical rents are sub-optimal, additional countries can receive differential pricing if they undertake serious measures to segment and protect the local elite market.[153] As the AIDS epidemic expands in Eastern Europe and Central Asia, access must be expanded to regions beyond sub-Saharan Africa.

Given the apparent limitations of the efficacy of voluntary pricing, it is important that compulsory licensing be more than a threat—that it be a viable way for countries to introduce generic competition. However, lack of manufacturing capacity in the lowest income countries limits the practicability of domestic production of generic pharmaceuticals. The TRIPS Agreement seemingly restricts compulsory licenses predominantly to domestic use, effectively preventing exports.[154] 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.[155] For example, compulsory licenses are arguably not useful to Malawi absent the opportunity to import from other countries, such as 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 United States conceded the point. Under the Cancun General Council Decision, the WTO now permits exports of compulsory licensed drugs to the poorest countries—an important development if compulsory licensing is to be a meaningful option for countries without manufacturing capacity.[156] The Cancun General Council Decision established a WTO notification process for cross-border compulsory licenses: The TRIPS Council must be notified, but WTO approval is not required.[157] In May 2004, Canada amended the Canadian Patent Law to permit compulsory

152. CBO, INCREASED COMPETITION, *supra* note 65, at xiii.

153. *See infra* Part II.

154. TRIPS Agreement, *supra* note 1, art. 31(f).

155. *See Doha Declaration on TRIPS*, *supra* note 32, ¶ 6.

156. *Cancun General Council Decision*, *supra* note 137; EU, Cancun, *supra* note 137. While the Cancun General Council Decision has the potential to positively impact access, it has not yet had an effect on drug availability. *See infra* note 293 and accompanying text.

157. *Cancun General Council Decision*, *supra* note 137, ¶ 2; *see also* EU, Cancun, *supra* note 137 (noting that WTO approval is not required).

licenses for certain drug exports to needy nations.[158] As of September 2004, no WTO Member has notified the TRIPS Council.[159]

Phil Thorpe's study on TRIPS implementation recently found that most developing countries have not taken advantage of the flexibilities and exceptions permitted under TRIPS.[160] He does not explore the reasons behind this failure, but two are likely. First, many countries may lack the impartial technical assistance needed to implement these provisions, including restrictions on "new use" patents, Bolar provisions, and international exhaustion rules. When the World Intellectual Property Association has provided assistance, developing countries have found WIPO's agenda to be IP maximalist rather than aimed at taking full advantage of TRIPS flexibilities.[161] Second, the TRIPS-plus[162] offensive of the U.S. Trade Representative (USTR) and the "Special 301" reports from that same office are frequently used to bluster countries into modifying

158. The Jean Chretien Pledge to Africa Act, House of Commons, 3d Sess., 37th Parliament, 52-53 Eliz. II, 2004 (Bill C-9) (received Royal Assent on 14 May 2004) [hereinafter Canadian Bill C-9]. The law created a positive list of drugs eligible for compulsory licensure, a procedural hurdle not required by the WTO. *Id.* Sched. 1. France and Noway have recently followed suit. Law. N. 2004-800, Aug. 6, 2004, J.O, Aug. 7, 2004, p. 18 (Fr); Regulations Amending the Patent Regulations (In Accordance With the Decision of the WTO General Council of 30 August 2003, Paragraphs 1(b) and 2(a)), Royal Decree of 14 May, 2004 (Nor.), http://www.cptech.org/ip/health [hereinafter Norwegian Compulsory License Regulation]. Norway does not have a significant pharmaceutical sector, so the impact of the regulation is modest. *Id.* ¶ 7 (official explanation of the regulation). Canada is more likely to actually export, but the Canadian law is more restrictive than the Norwegian. *See* CANADIAN HIV/AIDS LEGAL NETWORK, GLOBAL ACCESS TO TREATMENT: CANADA'S BILL C-9 AND THE COMPULSORY LICENSING OF PHARMACEUTICALS FOR EXPORT TO COUNTRIES IN NEED (2004), http://www.aidslaw.ca/Maincontent/issues/cts/patent-amend/billC-9flyer300604.pdf. The Norwegian regulations are far less restrictive.

159. The WTO has established a web page 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 September 28, 2004.

160. THORPE, *supra* note 32, at 1.

161. Public comments by the official delegations from several non-OECD countries at the Trans Atlantic Consumer Dialogue Future of WIPO Workshop, Geneva (Sept. 13, 2004) (the author was present); *see also* Geneva Declaration on the Future of the World Intellectual Property Organization, http://www.cptech.org/ip/wipo/futureofwipo declaration.pdf (last visited Sept. 21, 2004) ("The WIPO technical assistance programs must be fundamentally reformed.").

162. "TRIPS Plus" refers to provisions which exceed the floors established under the TRIPS Agreement.

domestic law to the liking of U.S. owners of IP. WTO Members should have a realistic opportunity to implement the flexibilities bargained for in TRIPS, including compulsory licensure, unhindered by unilateral U.S. interests.

b. Compulsory Licensing Need Not Harm Optimal Innovation

Assuming that production for compulsory licensure is limited to non-commercial markets, production by a third party does not add any marginal cost to the innovator and, thus, will not impede innovation.[163] If global pharmaceutical rents are supra-optimal, then compulsory licenses without royalties can be utilized without loss of innovation incentives. The burden of proof of sub-optimality should be on the innovator companies seeking a royalty, and the royalty rate in conditions of sub-optimality should balance innovation and access goals. In all cases, such nonrival use by low income populations should be viewed as an opportunity rather than a problem.[164]

A free rider problem may emerge if compulsory licensure decisions are evaluated solely at the domestic level. Each country may rationally choose to shirk its share of R&D costs, the same free rider problem afflicting innovation generally. Some form of global coordination may be required to address the negative externality.[165] Second-degree price discrimination such as price controls or other domestic rules affecting the ability of companies to appropriate rents also raise global coordination issues, which are now being negotiated in U.S. bilateral free trade agreements.[166]

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163. This result holds without regard for whether rents are currently supra- 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 CAL. L. REV. 1293 (1996) (arguing that compulsory licenses in digital media are less efficient than private contractual efforts).

164. Scherer, *Global Welfare*, *supra* note 135, at 1141.

165. This is particularly true amongst the OECD, where free riding has the greatest potential to affect global rents. *See infra* Section II.B.

166. BUDDHIMA LOKUGE & THOMAS FAUNCE, TRADE DISPUTES AND THE PHARMACEUTICAL BENEFITS SCHEME: CONSTRUCTIVE AMBIGUITIES, NON-VIOLATION NULLIFICATION DISPUTES AND THE AUSTRALIA US FREE TRADE AGREEMENT 8-9 (Austl. Nat'l Univ., Informal Working Paper, Sept. 2004) (on file with author).

ii. Dysfunctional Pharmaceutical Arbitrage

The second implication of global optimality concerns dysfunctional pharmaceutical arbitrage. The form of pharmaceutical arbitrage which is most likely to reduce rents is diversion from charitable non-commercial markets into high income markets.[167] If global pharmaceutical rents are sub-optimal (or made sub-optimal thereby), this arbitrage may be labeled dysfunctional. The EU recognizes that its attempts to support differential pricing for essential medicines depend in part upon blocking arbitrage into high income markets.[168]

It is important to note the limited scope of the case against dysfunctional pharmaceutical arbitrage. It does not apply to generic drugs because protecting the generic company's profits will not create incentives for innovative R&D, and thus arbitrage restrictions on generic drugs are not supportable on innovation grounds.[169]

Restrictions are also inappropriate between and to low income markets, so long as commercial markets are not replaced. Arbitrage restrictions could be lifted on sales to and within low and medium income countries. Outside of high income markets, the international exhaustion rule should always apply, as there is no proven innovation-based warrant for denying nonrival access.

Some level of arbitrage to recent immigrants to high income countries might be tolerable. Very little money is at stake for PhRMA companies and the likely high income country consumers of smuggled African drugs might well be at the margins of the country's health care system. Recent immigrants may not be full market participants either, despite their physical location in a high income country. The well-publicized confiscation of thirty-six thousand packages of African AIDS medications in the Netherlands in October 2002 might fit this profile.[170] Even if the

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167. Parallel trade from poor countries to rich countries is incompatible with differential pricing of essential medicines. *See* DANZON & TOWSE, *supra* note 12 (noting that parallel trade defeats the objectives of differential pricing); David A. Malueg & Marius Schwartz, *Parallel Imports, Demand Dispersion, and International Price Discrimination*, 37 J. INT'L ECON. 167, 193 (1994).

168. DG TRADE, *supra* note 42, at 2.

169. Restrictions might be appropriate on other grounds, such as safety. If a generic drug has not been approved in a market, importing it would not be arbitrage. For unpatented or generic products, no innovation-based case for banning parallel trade can be offered.

170. DUKES, *supra* note 84, at 50 n.1. For surprising details on this case, see *infra* notes 313-323 and accompanying text.

patients are market participants, receiving familiar medications from home, in their native language, might well be the best medical practice. In the United States, the uniform use of English labels in a multicultural society is not a culturally competent practice for recent immigrants lacking good English skills.

Arbitrage controls may be unnecessary between and within high income markets if pharmaceutical rents are supra-optimal. Put another way, parallel trade in patented pharmaceuticals within high income markets may be permitted.[171] If rents are sub-optimal, the domestic exhaustion rule should apply in high income markets, forbidding parallel imports into such countries and raising pharmaceutical rents. Otherwise, the international exhaustion rule should apply to sales between high income markets on free trade principles since consumers will benefit while innovation incentives remain intact.

iii. Domestic Pharmaceutical Arbitrage

The current TRIPS approach is tied to state sovereignty, affecting legal regimes along national political boundaries. TRIPS aggregates customers into country-level markets, reflecting both transaction costs and the political realities of sovereignty. This state-centric system is not surprising, given that only states are WTO Members, but the process suffers from both over-inclusion and under-inclusion.

Over-inclusion occurs when an entire country is granted an exception, extension, or flexibility under TRIPS, even though some people within these low or middle income countries can afford to pay high income market prices for drugs. Even in the poorest countries, an elite cadre of individuals control enough wealth to afford these drugs. In middle income countries such as India, Brazil, Chile, Mexico, South Africa, China, and Argentina, these markets are significant and growing.[172] The elites in low

171. Pharmaceutical arbitrage within high income markets is the subject of Section II.B on Canadian-U.S. pharmaceutical arbitrage.

172. In its 2001 submission to the United States Trade Representative, PhRMA claimed that $260 million was lost annually due to unlicensed generic drug products in Argentina. Sell, TRIPS, *supra* note 142, at 496 n.55 (citing PHARM. RESEARCH MFRS. OF AM., NATIONAL TRADE ESTIMATE REPORT ON FOREIGN TRADE BARRIERS (2001)). In 2003, the pharmaceutical industry's estimate ballooned to $600 million and was included in the 2003 National Trade Estimate Report without any apparent verification from outside of the industry. U.S. OFFICE OF TRADE REPRESENTATIVE, 2003 NATIONAL TRADE ESTIMATE REPORT ON FOREIGN TRADE BARRIERS, ARGENTINA 6 (2003), http://www.ustr.gov/assets/Document_Library/Reports_Publications/2003/2003_NTE_Report/asset_upload_file997_6178.pdf. The estimate was

and middle income countries are actually part of the high income market and should be expected to participate in this market on normal commercial terms.[173]

Theory suggests that providing low-cost AIDS drugs to impoverished South Africans might make it more difficult to charge full price to wealthy or middle class South Africans, but apparently PhRMA companies effectively segment these markets,[174] much as they do in the United

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dropped from the 2004 National Trade Estimate Report. U.S. OFFICE OF TRADE REPRESENTATIVE, 2004 NATIONAL TRADE ESTIMATE REPORT ON FOREIGN TRADE BARRIERS, ARGENTINA (2004), http://www.ustr.gov/assets/Document_Library/Reports_Publications/2004/2004_National_Trade_Estimate/2004_NTE_Report/asset_upload_file568_4735.pdf.

173. Pharmaceutical companies may currently prefer to keep the small full-priced elite market in developing countries rather than risk arbitrage. FREDERICK M. SCHERER & JAYASHREE WATAL, WHO COMM'N ON MACROECONOMICS & HEALTH, POST-TRIPS OPTIONS FOR ACCESS TO PATENTED MEDICINES FOR DEVELOPING COUNTRIES (2001) [hereinafter SCHERER & WATAL, POST-TRIPS OPTIONS]; Oxfam, *Fatal Side Effects: Medicine Patents Under the Microscope*, *in* ECONOMICS OF ESSENTIAL MEDICINES, *supra* note 3, 81, 93 (suggesting drug companies profit from elite households in Argentina, Brazil, India, and China); W. Duncan Reekie, *The Development Trilemma and the South African Response*, *in* THE ECONOMICS OF ESSENTIAL MEDICINES, *supra* note 3, at 167-68 (showing that the top twenty percent of South Africans enjoy a per capita GNP of $27,699, comparable to OECD levels and are therefore a significant market for drug companies); World Health Organization-World Trade Organization, *Differential Pricing and the Financing of Essential Drugs*, *in* ECONOMICS OF ESSENTIAL MEDICINES, *supra* note 3, at 213 (recognizing elite drug markets in developing nations); Patricia Danzon & Michael Furukawa, Prices and Availability of Pharmaceuticals: Evidence from Nine Countries exhibit 8 (undated presentation), *at* http://hc.wharton.upenn.edu/danzon/index.htm (showing that prices normalized by national income in Chile and Mexico are at 528% and 529% of the U.S. prices, which I interpret 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 U.S. Securities and Exchange Commission, PhRMA companies acknowledge the growing middle class markets in the developing world. Merck & Co, Inc., SEC Form 10-k, at 14 (filed Mar. 10, 2004) [hereinafter Merck, SEC Form 10-k]. PhRMA companies have recognized the potential of these markets for some time. *Foreign Trade Practices (Part 2): Hearing Before the Subcomm. on Oversight and Investigations, and the House Comm. on Energy and Commerce*, 99th Cong. 196 (1985) (statement of Gerald Mossinghoff, PhRMA President).

174. 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. MSF, SURMOUNTING CHALLENGES, *supra* note 141, at 37. A recent WHO survey found significant variations in prices of essential medications within most countries surveyed. Jeanne Madden, *Basic Results That the WHO/HAI Survey Offers Country-Level Investigators*, 33 ESSENTIAL DRUG MONITOR 15 (2003). Significant domestic price variations indicate that various legal and market-based segmentation approaches were apparently

States.[175] The persistence of domestic differential pricing, even in the face of extensive donor programs, is a testament to the effectiveness of market segmentation by PhRMA companies and the apparent weakness of actual pharmaceutical arbitrage pressure. Possible mechanisms are brand campaigns with trademarks, differential pricing by payor, and domestic legal restrictions on arbitrage.[176]

Under-inclusion occurs when a middle income country does not qualify for exceptions or flexibilities, or is discouraged from taking advantage of them, despite the needs of some desperately poor citizens therein.[177] The state-centric system lays responsibility for low income patients on the middle and high income countries in which they reside. Here we see a weakness of any system of defining market segments by state political borders rather than actual health needs or ability to afford medicines. It also illustrates the arbitrary categories of development and the difficulties a country might face when it 'graduates' to a higher category.

Accommodations (such as nonrival access to low income populations) may be offered to middle income countries without damaging innovation, so long as domestic price discrimination legal structures are successfully maintained.[178] Again, if global pharmaceutical rents are supra-optimal, PhRMA companies could bear the loss of some elite markets without harming innovation.

A simple estimate in the case of HIV drugs may be useful: PhRMA would likely not suffer significant lost profit if all sales of HIV products in

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functioning.

175. *See* W. VA. PHARM. COST MGMT. COUNCIL, REFERENCE PRICING SUBCOMMITTEE 2-3, app. A-1, A-2 (2004) (demonstrating significant price discrimination within West Virginia between prescription drug prices under Medicaid, private payors, the Public Health Service's 340b program, and the Federal Supply Schedule, as well as Canadian and Australian prices) [hereinafter WEST VIRGINIA REPORT], http://www.wvc.state.wv.us/got/pharmacycouncil/default.cfm.

176. Within the U.S. market, internal diversion is illegal in many cases. *See* Heather Won Tesoriero & Gary Fields, *FBI, FDA Investigates Big Drug Wholesaler*, WALL ST. J., Sept. 19, 2003, at B1 (reporting alleged diversion from discounted hospital markets to higher-priced secondary markets).

177. *See, e.g.*, Letter to Jong-Wook Lee, Director General, World Health Organization, and Peter Piot, Executive Director, Joint United Nations Programme on HIV/AIDS (Apr. 5, 2004), http://www.aidsinfonyc.org/tag/activism/UNltrOnPriceReductions.html (discussing the plight of lower middle income countries such as Egypt, Ukraine, Costa Rica, El Salvador, and Panama where ARVs are priced at unaffordable levels).

178. For a discussion of these legal structures, see *supra* Section I.C.

every low and middle income country dropped to zero. GlaxoSmithKline, the largest participant in the market for HIV drugs, reports sales in three geographic regions: the United States, Europe, and "International." This latter category includes high income countries such as Japan, Canada and Australia, as well as low and middle income countries in Latin America, Asia, Africa and the Middle East. Even so, total international HIV drug sales in 2003 were only £155 million,[179] in a year in which gross profit was £17.2 billion and selling, general, and administrative (SG&A) expenses were £7.5 billion. Actual profits from ARV sales in both low and middle income markets are likely to be negligible to GSK's global profits and R&D, particularly if elite markets in these countries remain commercial.

iv. Optimizing Subsidies

Another form of optimization creates subsidies to achieve particular goals. Push subsidies include tax credits for R&D, general research grants such as those distributed by the United States's National Institutes of Health (NIH), and the orphan drug tax credit. Pull subsidies directly address the issue of the appropriation of rents; such mechanisms include the patent system, exclusive marketing periods for orphan and pediatric drugs, and donor purchase commitments for development of a specific pharmaceutical, such as an AIDS or malaria vaccine[180] or antidotes to bioterrorism.[181]

The heuristic suggests three implications. First, for drugs or conditions with sub-optimal pharmaceutical rents, government intervention should increase pharmaceutical rents toward optimal levels. For example, subsidies are essential for neglected diseases, where the target population cannot afford any commercial price for therapy. Second, subsidies can be limited to drugs with sub-optimal pharmaceutical rents without harming innovation. Scarce subsidies should not be directed to drugs with strong commercial potential, but should be reserved for neglected diseases.

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179. GLAXOSMITHKLINE PLC, 2003 ANNUAL REPORT, Form 20-F, at 61-63.

180. Michael Kremer, *Pharmaceuticals and the Developing World*, 16 J. ECON. PERSP. 67, 82-85 (2002). For a recent example, see Press Release, Inst. for OneWorld Health, Institute for OneWorld Health Receives Gates Foundation Grant to Fund Development of Malaria Vaccine (July 13, 2004), http://www.oneworldhealth.org/media/details.php?prID=76.

181. 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 1 (Cong. Research Serv. Report for Congress, RS21507, 2003). The proposed size of the pull subsidy for bioterror countermeasures is $5.593 billion through FY 2013. *Id.* at 3.

Finally, for patented drugs with supra-optimal pharmaceutical rents, the government may intervene to achieve other goals, such as improved nonrival access, without undermining R&D innovation.

Applying these implications to recent policy proposals is instructive. Frederic M. Scherer and Jayashree Watal have proposed expanding U.S. tax incentives for donating pharmaceuticals to poor countries,[182] but this additional push subsidy is warranted only if pharmaceutical rents are sub-optimal. Likewise, the U.S. Congress on September 23, 2004 authorized $7.6 billion to extend the expiring R&D tax credit for another eighteen months without targeting specific disease conditions.[183] Proposals for indiscriminate tax credits are unsupported absent evidence of sub-optimality of global pharmaceutical rents.

v. National Drug Regulation and WHO Prequalification

National regimes for testing the safety and efficacy of patented drugs are inefficient, duplicating scientific work and wasting resources unnecessarily. Each New Chemical Entity (NCE) requires clearance by the FDA in the United States and parallel regulatory authorities in every country where the drug will be sold. Prior to the establishment of the EMEA,[184] some estimates put the cost of duplicative NDRA processes within the EU at £500 million per year.[185] NDRA rules also delay the launch of innovative drugs in many countries.[186] A "reference" approval process would reduce duplicative costs and speed market entry of pharmaceuticals.[187]

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182. SCHERER & WATAL, POST-TRIPS OPTIONS, *supra* note 173.

183. Working Families Tax Relief Act of 2004, Pub. L. No. 108-311, §301(1), 118 Stat. 1166 (2004) (conference report approved by House and Senate, Sept. 23, 2004); Rob Wells & Maya Jackson Randall, *Tax-Cut Bill Aids Firms; Research Credit Extended,* WALL ST. J., Sept. 27, 2004, at A5.

184. Council Regulation 2309/93, O.J. (L 214), as amended by Commission Regulation 649/98 O.J. (L 88) 7.

185. ROTHNIE, *supra* note 66, at 493-94 (citing various sources).

186. *See* PATRICIA M. DANZON ET AL., 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, 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 rents are supra-optimal, this industry practice is reprehensible, as it voluntarily withholds important drugs from patients.

187. Many NDRAs practice a form of reference approval when they require, as a

A reference approval system requires at least four provisions. First, safety and efficacy testing would be referenced against approval in certain benchmark countries. For example, if a compound was approved as safe and efficacious by either the U.S. FDA or the EU's EMEA, then it could automatically be deemed to meet standards in the target country. Second, WHO prequalification (or a similar process) would be deemed to satisfy other domestic NDRA requirements, such as bioequivalence for generic entry and good manufacturing practices. Third, IP rights and drug marketing approvals should also be de-linked. IP rights would still be enforceable under domestic law and TRIPS, but NDRA approval should proceed apace. Finally, in categories of strong local collective preference (such as RU-486), the NDRA may retain a veto.

The United States opposes the first three of these elements, without an innovation warrant. Expansion of the WHO prequalification process is a clear example. WHO Prequalification is clearly useful in many regions, with many different companies producing generic ARVs under unknown conditions.[188] In the 2004 World Health Assembly, the United States pushed to remove the word "strengthening" from the WHO HIV/AIDS Resolution concerning prequalification.[189] The word was retained in the final document,[190] but the United States continues to marginalize the prequalification process in PEPFAR.[191] The United States also implicitly opposed reference approvals in various free trade agreements, on the ground that the rights of data exclusivity must be protected.[192] The recent

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condition of application for marketing approval, prior marketing approval in either the United States., the EU, or Japan. My suggestion is that NDRAs could consider extending the practice for all of the biological aspects of the marketing approval process, retaining only the right to veto based on a collective preference, as well as approval of the labeling.

188. AM. FOUND. FOR AIDS RESEARCH, TREAT ASIA SPECIAL REPORT: EXPANDED AVAILABILITY OF HIV/AIDS DRUGS IN ASIA CREATES URGENT NEED FOR TRAINED DOCTORS 4 (2004), http://www.amfAR.org/treatment/news/TADoc7.pdf [hereinafter AmfAR].

189. *Compare* World Health Org., A57/A/Conf.Paper No. 3 Rev. 1(May 20, 2004), *with* Rev.2 (May 21, 2004).

190. *Scaling up Treatment and Care Within a Coordinated and Comprehensive Response to HIV/AIDS*, World Health Assembly, 57th Ass., Agenda Item 12.1, at 3, WHO Doc. WHA57.14 (May 22, 2004) [hereinafter World Health Assembly, *Scaling up Treatment*].

191. Marilyn Chase, *Generic AIDS Pill Gets Acceptance*, WALL ST. J., July 2, 2004, at B3.

192. MÉDECINS SANS FRONTIÈRES, MSF BRIEFING NOTE, ACCESS TO MEDICINES AT RISK ACROSS THE GLOBE: WHAT TO WATCH OUT FOR IN FREE TRADE AGREEMENTS WITH THE UNITED STATES 4-6 (2004), http://www.accessmed-msf.org/documents/ftabriefingenglish.pdf [herinafter MSF, FREE TRADE AGREEMENTS]; DAVID VIVAS-EUGUI, QUAKER U.N. OFFICE, REGIONAL AND BILATERAL AGREEMENTS AND A TRIPS-PLUS WORLD: THE FREE TRADE AREA OF THE AMERICAS

Free Trade Agreement (FTA) with Australia requires linkage between drug approval and patent status for the first time, exporting a portion of Hatch-Waxman to Australia.[193]

Resources are also wasted in the generic entry process. NDRAs should not require generic applicants to repeat any clinical studies without a clear benefit to public health.[194] Generic companies also expend resources to reverse-engineer patented drugs. Reverse-engineering in this case is a wasteful effort and needlessly delays launch in low income countries by several years.[195] The United States's TRIPS-plus proposals to extend data exclusivity to five or ten years[196] will further increase costs and delay generic entry. If pharmaceutical rents are already supra-optimal, all of this is a social loss. Taking unnecessary costs out of the NDRA system makes R&D more efficient, lowers the threshold for cost-effective innovation, and delivers innovative drugs to patients more quickly.

vi. Price Controls

This Article is agnostic on the question of the desirability of pharmaceutical price controls generally. 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 heuristic suggests five conclusions about pharmaceutical price controls. It confirms three relatively uncontroversial points: (1) price

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(FTAA) 16-18 (2003) (on file with author) [hereinafter VIVAS-EUGUI, QUAKER UN OFFICE].

193. M. Kevin Outterson, *Free Trade in Pharmaceuticals*, 181 MED. J. AUSTL. 260-61 (2004); Ken J. Harvey et al., *Will the Australia-United States Free Trade Agreement Undermine the Pharmaceutical Benefits Scheme?*, 181 MED. J. AUSTL. 256-59 (2004).

194. PhRMA companies withhold much of this data as trade secrets or seek "data exclusivity" to block generic entry, but when a patent is set to expire there is no innovation warrant to delay generic entry, unless all generic entry is premature.

195. Watal reports a lag of about two years for generic pharmaceuticals reverse-engineered in India. Jayashree Watal, *Pharmaceutical Patents, Prices and Welfare Losses: Policy Options for India Under the WTO TRIPS Agreement*, 23 WORLD ECON. 733-52 (2000).

196. MSF, FREE TRADE AGREEMENTS, *supra* note 192, at 4-6; OXFAM INT'L, UNDERMINING ACCESS TO MEDICINES: COMPARISONS OF FIVE US FTA'S 13-15 (Oxfam Briefing Note, 2004); VIVAS-EUGUI, QUAKER UN OFFICE, *supra* note 192, at 16-18. The United States is currently pressuring Israel to accept five to ten years of data exclusivity, a threat targeting Teva Pharmaceuticals, one of the world's largest producers of generic medicines, based in Israel. *Teva Opposes 10-Year Data Exclusivity Provision for Israel*, 21 GENERIC LINE, May 5, 2004, 2004 WL 65711471; Hadas Manor, *US to Israel: Grant 5-Year Exclusivity for Ethical Drugs*, GLOBES (Israel), (July 1, 2004), http://www.globes.co.il/serveen/globes/docview.asp?did=810543&fid=942.

controls should exclude generic products; (2) developing country differential prices should not be used in high income country external reference pricing systems; and (3) price controls should be stable over long periods of time. The last two conclusions are likely to meet more controversy: (4) optimization of rents is preferable to price-fixing and reference pricing; and (5) PhRMA company data should be more transparent on a global basis.

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 to patented drugs. Generic products do not generate patent rents, and thus should be exempt.[197]

Second, virtual forms of dysfunctional arbitrage must be blocked. High income markets should not utilize developing country differential prices as an external reference price within these countries.[198] At present, this is not a problem, as it appears that no high income country uses donor prices in its reference pricing system.

Third, 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 signals for the political risk of more onerous price controls.

Fourth, the heuristic prefers optimization over price-fixing and

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197. Internal reference pricing systems may 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.

198. F.M. Scherer & Jayashree Watal, *The Economics of TRIPS Options for Access to Medicines*, *in* ECONOMICS OF ESSENTIAL MEDICINES, *supra* note 3, at 32, 48-49 (arguing for a ban on external reference pricing which uses prices in low income nations). Just like physical arbitrage, this practice should be restricted only when it flows from poor to rich nations. External reference pricing within high income countries, or within low and middle income countries does not undermine differential pricing for the poor. *But see* Scherer & Watal, *supra*, at 49 (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 12, at 6, 16-17. Their solution is vigorously rejected by Médecins sans Frontières, which has been very active in negotiating price discounts and distributing ARVs in sub-Saharan Africa. MSF, UNTANGLING THE WEB, *supra* note 151; MSF, SURMOUNTING CHALLENGES, *supra* note 141, at 7.

reference pricing. In this context, the policy goal should be to take the widest possible advantage of nonrival access, limited only by setting the minimum level of rents necessary to ensure optimal R&D. Any modifications to the strength of the power to appropriate rents must be evaluated in this light, whether it falls in the domain of IP law, contract, market regulation, national drug regulation, or trade agreements.

By contrast, price-fixing implies a price level without considering these other issues. Reference pricing schemes also may proceed automatically. By contrast, the reimbursement systems in Australia and the United Kingdom illustrate two different optimization approaches which support innovation.

In Australia's Pharmaceutical Benefits Scheme (PBS), each new drug must be approved under an economic evaluation process if governmental reimbursement is desired. The company must submit a dossier to the Pharmaceutical Benefits Advisory Committee (PBAC) proposing a price for the drug and supporting the economic efficiency of that price, given the drug's clinical advantages over existing therapies. In other words, Australia pays for value: Highly innovative drugs receive a much higher price; me-too drugs are priced with the lowest-cost equivalent. The incentives are obvious.[199]

The United Kingdom's National Institute of Clinical Effectiveness (NICE) also performs economic evaluation of drugs, but targets a drug company's UK return on investment for its drug portfolio to the FTSE 100 London stock market index. One can argue about transfer pricing games and whether the FTSE 100 is an appropriate target, but the overall structure of the program is designed to support a reasonable return on R&D investment.[200]

Finally, greater transparency is warranted. Although biological data from clinical trials is generally applicable worldwide, many NDRAs accept confidentiality restrictions on data submitted for marketing approval and

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199. LOKUGE & FAUNCE, *supra* note 166, at 7-8; SANJOY ROY, W. VA. PHARM. COST MGMT. COUNCIL, AN OVERVIEW OF PHARMACEUTICAL REFERENCE PRICING AND REIMBURSEMENT: ANALYSIS OF THE AUSTRALIAN PHARMACEUTICAL BENEFITS SCHEME 12-23 (2004), http://www.wvc.state.wv.us/got/pharmacycouncil/default.cfm.

200. JOAN-RAMON BORRELL, PRICES OF MEDICINES: A CASE-STUDY OF THE IMPACT OF THE RATE-OF-RETURN REGULATION IN THE UNITED KINGDOM 22 (Univ. of Barcelona Working Paper, 1997) (finding the regulation largely ineffective in controlling UK medicine prices); SARAH F. JAGGAR, GEN. ACCOUNTING OFFICE, GAO/HEHS-94-30, PRESCRIPTION DRUGS: SPENDING CONTROLS IN FOUR EUROPEAN COUNTRIES 69-77 (1994) (France, Germany, Sweden, and the United Kingdom).

reimbursement, needlessly reinventing the wheel each time. These unnecessary costs raise rents without social benefit. The economic evaluation studies submitted to the Australian PBAC would be very helpful in formulary and reimbursement decisions worldwide.[201] Further, if certain forms of price controls are adopted, optimizing pharmaceutical rents will require accurate global data on pharmaceutical pricing, profitability, and innovation. This information is not currently available to independent researchers, forcing policy makers to rely on the DiMasi study of secret and unverified industry data.[202] It strains credulity to base important pharmaceutical policy decisions on secret industry data, unavailable for study by other researchers.

vii. Free Riders

The heuristic has additional implications for the free rider problem in pharmaceutical innovation. If the free rider is a low income country (or low income person), we can consider the situation either a gift or harmless nonrival use.[203] Free riding by high income countries is a more complicated problem.

Most high income countries have created direct or indirect governmental reimbursement of prescription drugs. One cannot expect governments to passively accept third degree differential pricing dictated by the drug companies. Nor do governments accept Ramsey Optimal Pricing based upon the government's ability to pay. Governmental resources are too scarce to completely resist the monopsony power, with the possible (temporary) exception of the United States.[204]

Acting solely in the national interest, governments may negotiate for the lowest possible prices, unconcerned about the possible negative global

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201. Outterson, *supra* note 193, at 260-61.

202. DiMasi et al., *supra* note 29. The R&D expenditure data source for this study was a "confidential survey" returned from ten PhRMA companies, *id.* at 152, 156, as well as unverified PhRMA aggregate data, *id.* at 179.

203. Scherer, *Global Welfare*, *supra* note 135, at 1141.

204. The federal government is prohibited from exercising monopsony powers in the new Medicare Part D drug benefit. Medicare Prescription Drug Improvement and Modernization Act of 2003, Pub. L. No. 108-173, § 301, 117 Stat 2066 (to be codified at § 1808(c)(1)(C) of the Social Security Act, 42 U.S.C. 139b-9). 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.

effects on innovation. PhRMA companies may respond by raising prices in uncontrolled markets. The United States is the largest such market. Put bluntly, high income countries with price controls are said to be free riders on American innovation.[205]

Whether the free rider thesis is true empirically is an open question.[206] Perhaps the crusade against the scourge of low-priced drugs is misplaced. Perhaps American prices are supra-optimal, and Canadian prices are optimal.[207] Other countries may make up for their lower prices with higher volumes, eliminating the free rider problem. In many EU countries, drug prices are lower but account for a higher percentage of health expenditure than in the United States.[208] It may be unfair to label such countries as free riders. Empirical doubts are also raised when the United States tolerates significant domestic free riders without apparent harm. Canadian prices are similar to the Federal Supply Schedule. Some Medicaid rebates and the U.S. Public Health Service's 340b program get better deals than Australia or Canada.[209] Before one picks up stones to cast, check the glazing at home. PhRMA companies act as if the empirical question is beyond doubt, proceeding apace to the solution phase. Answering these questions properly requires transparent access to confidential company data. In any event, free riding is an innovation problem only if global pharmaceutical rents are sub-optimal.

The current PhRMA company solution is to use U.S. free trade agreements to raise drug prices outside of the United States.[210] To this end,

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205. U.S. Editorial, *Lower US Prices Through Higher International Prices*, 9 PHARMA PRICING & REIMBURSEMENT 222 (2004).

206. Kevin Outterson, *Free Trade Against Free Riders?*, 9 PHARMA PRICING & REIMBURSEMENT 254-55 (2004).

207. I thank Professor Jim Friedberg for this suggestion. The free rider hypothesis assumes a joint sunk cost, but another possibility is that lower-priced countries such as Canada are efficiently avoiding waste. One empirical study suggests that PhRMA companies still make sufficient profits on Canadian sales, undercutting the free rider hypothesis. SAGER & SOCOLAR, *supra* note 11, at 1.

208. ORG. FOR ECON. COOPERATION AND DEV., OECD HEALTH DATA 2004, tbl.14 (2004), http://www.oecd.org/document/16/0,2340,en_2825_495642_2085200_1_1_1_1,00.html (noting that Canada, France, Germany, Switzerland, and the UK have higher total expenditures on pharmaceuticals as a percentage of total expenditure on health as compared to the United States).

209. WEST VIRGINIA REPORT, *supra* note 175, app. A-2, A-2 (comparing Medicaid, private payor, 340b, Canadian, FSS, and Australian data).

210. Peter Drahos & David Henry, *The Free Trade Agreement Between Australia and the United States: Undermines Australian Public Health and Protects U.S. Interests in Pharmaceuticals*, 328

USTR recently created the post of Assistant United States Trade Representative for Pharmaceutical Policy. Bilateral treaties are an awkward response to this global coordination problem. USTR may succeed in raising drug prices in the least appropriate places. The greatest success will be found in the poorest countries, or other smaller countries desperately seeking preferential access to the U.S. market.[211] Small, poor countries offered a free trade deal with the United States may well agree to provisions which undermine health in order to serve commercial interests. But these small and generally poor markets can make very little contribution to the global fight against pharmaceutical free riders. The U.S. stance should be the opposite: Low income markets are the best targets for the enlightened policy of nonrival access.

If the USTR's solution is to be significant for innovation, it must involve the EU and Japan, but the USTR will find them better positioned to resist bilateral U.S. pressure to modify sensitive domestic health policy. Nor is there any guarantee that increased prices abroad will result in lower prices in the United States. A strategy which depends upon offending America's best trading partners should be preceded by proof that innovation and access will be improved. The ultimate free riders are counterfeiters, not governments, and any strategy to increase global pharmaceutical prices will increase the opportunity for counterfeits.[212]

BRIT. MED. J. 1271-72 (2004); Elizabeth Becker, *Drug Industry Seeks To Sway Prices Overseas*, N.Y. TIMES, Nov. 27, 2003, at A5; Elizabeth Becker & Robert Pear, *Trade Pact May Undercut Importing of Inexpensive Drugs*, N.Y. TIMES, July 12, 2004, at A1; Marilyn Werber Serafini, *Drug Prices: A New Tack*, NAT'L J., Apr. 17, 2004, at 1177 ("So [House Speaker] Hastert and [Senator] Kyl championed the novel idea that the key to lowering U.S. prescription drug prices is to persuade foreign governments to raise their prices. . . .The idea of trying to level the international playing field on prescription drug pricing originated with the U.S. pharmaceutical industry. But Hastert and Kyl played significant roles last fall in persuading the Bush administration to embrace this strategy. . . .The result was the United States' first free-trade agreement that included modest concessions on pharmaceutical price controls."); Marilyn Werber Serafini, *The Other Drug War*, NAT'L J., Mar. 20, 2004, at 871-72; Mark B. McClellan, Speech Before the First International Colloquium on Generic Medicine (Sept. 25, 2003), http://www.fda.gov/oc/speeches/2003/genericdrug0925.html.

McClellan's speech was widely reported. *See, e.g.*, Christopher Bowe & Geoff Dyer, *Americans Lured by Lower Prices*, FIN. TIMES, May 5, 2004, at 17 ("The rhetoric intensified in September when Mark McClellan, then head of the FDA, attacked European drug price controls and said other rich nations should pay more of the development cost for drugs.").

211. Witness the TRIPS-plus provisions in negotiated or pending FTAs with Morocco, Singapore, Jordan, Israel, Central America (CAFTA), and the Western Hemisphere (FTAA). *See supra* note 196 and accompanying text.

212. Aidan Hollis may well be the first to make this connection to counterfeiting explicit.

Other forms of global coordination should be considered, such as James Love and Tim Hubbard's Global R&D Treaty.[213] The R&D Treaty would serve as a global coordination mechanism amongst the high income countries, while permitting prices to decline to marginal manufacturing costs since R&D would no longer be recovered through the price mechanism. At lower price levels, access is greatly improved and the opportunity for counterfeits diminishes.

viii. Neglected and Global Diseases

a. Neglected Disease Innovation Does Not Require Increased Appropriation of Pharmaceutical Rents in Low Income Countries

Jean Lanjouw and Alan Sykes each support the enactment of IP laws in low income countries to encourage the development of local markets for treating neglected diseases.[214] 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),[215] but those NCEs are either me-too generics or target global diseases.[216] Sykes argues that the huge disease burden in the developing

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Aidan Hollis, An Efficient Reward System for Pharmaceutical Innovation (July 2, 2004) (discussing prizes based upon therapeutic value) (unpublished manuscript, on file with author) [hereinafter Hollis, Efficient Reward System]. *See infra* Subsection II.A.2 for a description of counterfeits.

213. JAMES LOVE, FROM TRIPS TO RIPS: A BETTER TRADE FRAMEWORK TO SUPPORT INNOVATION IN MEDICAL TECHNOLOGIES (Workshop on Economic Issues Related to Access to HIV/AIDS Care in Developing Countries, 2003); Hubbard, *supra* note 13; Love, *supra* note 13.

214. JEAN O. LANJOUW, A PATENT POLICY PROPOSAL FOR GLOBAL DISEASES 4 (The Brookings Institution, Working paper No. 84, 2001) (on file with author); Sykes, *supra* note 25, at 58-62.

215. JEAN O. LANJOUW, THE INTRODUCTION OF PHARMACEUTICAL PRODUCT PATENTS IN INDIA: 'HEARTLESS EXPLOITATION OF THE POOR AND SUFFERING?' (1998), http://papers.nber.org/papers/wb366.

216. 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) (finding that Indian companies are likely to target the largest markets, i.e., 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 generic pharmaceuticals. Adam Levitt, Dr. Reddy's Laboratories:

world should stimulate markets if patents were available. He 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.[217] Surely this burden should be imposed on the world's poorest people only as a last resort. We should not demand the widow's mite in order to fund PhRMA.

Moreover, strong IP laws in low income countries are simply and unfortunately insufficient 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.[218] An exclusive offer to sell drugs at a loss is not valuable.[219] Profit-maximizing Indian drug companies will focus

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Driving Growth 17-25 (Bear Stearns Healthcare Conference, Sept. 8, 2003) (on file with author) [hereinafter Levitt, Dr. Reddy's Laboratories]. The primary new drug application 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 rents to innovator companies through early generic entry by aggressive Indian companies.

217. Sykes, *supra* note 25, at 61-62. Notably, Sykes has critiqued F.M. Scherer on the question of the net value of IP laws for developing countries.

218. The relative size of the commercial and non-commercial markets is important here. The growth of India and China's middle and upper classes one day will be sufficient 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, SEC Form 10-k, *supra* note 173, 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.").

219. Keith E. Maskus, *Ensuring Access to Essential Medicines: Some Economic Considerations,* 20 WISC. INT'L L.J. 563, 574 (2002) (casting doubt on the efficacy of patents to improve R&D on neglected drugs); *see* Kettler & Modi, *supra* note 216, at 742 (noting that 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. JASON C. HSU & EDUARDO S. SCHWARTZ, A MODEL OF R&D VALUATION AND THE DESIGN OF RESEARCH INCENTIVES 37, 43-45 (Nat'l Bureau of Econ. Research, Working Paper No. 10041, 2003).

on their best economic opportunities;[220] neglected disease drugs will not be at the top of that list.[221] The leading Indian drug companies derive most of their profits from sales in the United States and other high income markets.[222] Nor are strong IP laws important to develop indigenous manufacturing capacity. The absence of pharmaceutical patents in India was the proximate cause of India's vibrant generic pharmaceutical sector. Implementation of TRIPS and restrictions on PEPFAR procurement will hinder this path of development.[223]

Developing non-OEDC pharmaceutical R&D capacity has the potential to improve the efficiency of global research. Non-OECD PhRMA companies may have significantly lower cost structures, enabling R&D on disease markets with less market potential. 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 may invest in regional markets heretofore overlooked by OECD

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220. Kettler & Modi, *supra* note 216, 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 United States and Europe or branded (generic) formulations sold in India and other similar markets. Levitt, Dr. Reddy's Laboratories, *supra* note 216, at 9-10.

221. Jean O. Lanjouw & Iain Cockburn, *New Pills for Poor People?: Empirical Evidence After GATT*, 29 WORLD DEV. 265, 265-89 (2001) (finding in 1998 survey of Indian drug firms that only 16% of the firms' 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 (FDC). CIPLA, SIXTY-SEVENTH ANNUAL REPORT 2002-2003, at 5 [hereinafter CIPLA 2002-2003 ANNUAL REPORT].

222. *See, e.g.*, CIPLA 2002-2003 ANNUAL REPORT, *supra* note 221, 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."); 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. For Dr. Reddy's Laboratories, the U.S. market accounted for fifty-seven percent of 2003 gross margin. Levitt, Dr. Reddy's Laboratories, *supra* note 216, at 11.

223. On PEPFAR procurement, see *infra* Subsection II.B.1.

companies[224] and invest in process developments to lower production costs.[225]

Most neglected disease conditions lack a market not because of the absence of IP rights in low income countries but because of the poverty of the patients. Perhaps the best description of a neglected disease drug is that market-based innovation is unlikely because the target population will require the drug or vaccine to be distributed at or below the lowest possible marginal cost of production. Any such drug will require non-market funding for innovation and distribution, with or without IP regimes.

Michael Kremer's model of a donor purchase commitment is a prominent example of a non-market mechanism,[226] attracting many commentators on the proper design of such a prize.[227] Prize systems and donor purchase commitments do not require IP laws in low income countries. The donor may reference the patent law of some country (such as the United States), without requiring the target populations to have any IP laws at all. The appropriate incentives are in place so long as the donor is bound to a credible commitment to act *as if* they are bound by the IP laws of a reference country such as the United States. This process would create a "reference" or "virtual" IP regime. This is a significant point, not well developed by supporters of TRIPS implementation in low income countries. Virtual IP regimes would achieve all of the claimed advantages of TRIPS implementation in low income countries for prizes, without the blocking effects of local IP laws.

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224. India, Russia, China, Brazil, Mexico, Africa, and other markets are major markets for Indian companies such as Dr. Reddy's Laboratories. Levitt, Dr. Reddy's Laboratories, *supra* note 216, at 17; *see also* Kettler & Modi, *supra* note 216, at 743 (describing the Indian pharmaceutical industry).

225. Kettler & Modi, *supra* note 216, at 743-45. But Kettler and Modi do not assume an Indian comparative advantage in cost.

226. Michael Kremer has thoughtfully analyzed and articulated the donor purchase commitment model. Michael Kremer, *Creating Markets for New Vaccines: Part I: Rationale & Part II: Design Issues*, *in* 1 INNOVATION POLICY AND THE ECONOMY 35-109 (Adam B. Jaffe et al. eds., 2001).

227. *See, e.g.*, Hollis, Efficient Reward System, *supra* note 212; Michael Abramowicz, *Perfecting Patent Prizes*, 56 VAND. L. REV. 115 (2003); Steven Shavell & Tanguy Van Ypersele, *Rewards Versus Intellectual Property Rights*, 44 J.L. & ECON. 525 (2001) (concluding that optional reward systems are superior to IP rights systems).

b. Global Disease Innovation Does Not Require Increased Appropriation of Pharmaceutical Rents in Low Income Countries

The neglected disease debate tends to overlook the fact that the chronic conditions of the high income and low income worlds are converging.[228] Global diseases[229]—conditions which affect patients in both rich and poor countries—include cancer and cardiovascular disease,[230] as well as AIDS.[231]

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228. Non-communicable disease accounts for forty-seven percent of the global burden of disease. WORLD HEALTH ORG., WHO GLOBAL STRATEGY ON DIET, PHYSICAL ACTIVITY AND HEALTH (May 22, 2004). Cancer and cardiovascular disease are the second and third largest causes of death in developing countries. WORLD HEALTH ORG., WORLD HEALTH REPORT 2003 (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. Response of the Research-Based Pharmaceutical Industry to the Interim Report of the Task Force on Access to Essential Medicines (Feb. 1, 2004), *reprinted in* DUKES, *supra* note 84, app. 2, at 7-8.

229. Herein, the term global disease refers to conditions for which a therapeutic market exists in high income countries, and the condition is also endemic to the low or middle income world. The definition of global disease is not static. Malaria was once a global disease, but is now largely eradicated in high income countries, rendering it neglected. Diseases may also move in the opposite direction. Increased international mobility is likely to further blur the epidemiological effect of political borders, causing neglected diseases to migrate into the global disease category. 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 et al., *Health-care System Frailties and Public Health Control of Communicable Disease on the European Union's New Eastern Border*, 363 THE LANCET 1389-92 (2004).

230. Carlos Correa interprets the *Doha Declaration* to include global diseases such as asthma and cancer. CORREA, IMPLICATIONS OF DOHA, *supra* note 137, 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).

231. North America and Western Europe account for less than two million of the thirty-four to forty-six 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 two market failures plague public health. First, one strain of AIDS (Type A) is largely confined to the developing world, and thus receives less research

As an example of crossover potential of global diseases, consider the WHO Prequalification Project. The WHO has requested prequalification dossiers on four cancer drugs (vinblastine, etoposide, bleomycin and vincristine)[232] and two have been prequalified.[233] These drugs are all related to the treatment of AIDS-related cancers and are off-patent in the United States.[234] For the treatment of TB, the WHO prequalified non-licensed generic forms of patented ciprofloxacin from India and Spain.[235] But these drugs may be used to treat conditions other than TB and AIDS related cancers.[236] The Doha Declaration was not limited to these three diseases, despite U.S. efforts to narrow the exception.[237]

To the pharmaceutical industry, extending nonrival access to global disease drugs outside of AIDS, malaria, and TB opens Pandora's Box. Roger Bate acknowledges that the United States negotiated to limit flexibilities to twenty two diseases, keeping "lifestyle complaints and major western diseases" off the table.[238] Nonrival access should not be limited to these three diseases, or narrow "on label" uses, but should be extended to any global disease, on the basis of global disease burden and public health need. Furthermore, this extension will not adversely affect innovation. The most important proposition about global diseases is that a robust level of

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attention. Second, pediatric AIDS is also primarily a developing country issue, including the debates over the use of Nevirapine and the absence of pediatric formulations of most AIDS drugs. MÉDECINS SANS FRONTIÈRES, UNTANGLING THE WEB OF PRICE REDUCTIONS: A PRICING GUIDE FOR THE PURCHASE OF ARVS FOR DEVELOPING COUNTRIES 5 (4th ed. 2003) ("Children living with HIV/AIDS are one of the most neglected populations: pediatric 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, and non-adapted dosages. For example there are currently no combinations for paediatric use.").

232. WORLD HEATH ORG., ACCESS TO HIV/AIDS DRUGS AND DIAGNOSTICS OF ACCEPTABLE QUALITY, PROCUREMENT QUALITY AND SOURCING PROJECT (15th ed. 2004) [hereinafter WHO HIV/AIDS PREQUALIFICATION, 15th ed.], http://mednet3.who.int/prequal/.

233. Those two drugs are vinblastine and vincristine. WHO HIV/AIDS PREQUALIFICATION, 15th ed., *supra* note 232.

234. FDA ORANGE BOOK (Oct. 2004), http://www.fda.gov/cder/ob/default.htm.

235. WHO HIV/AIDS PREQUALIFICATION, 15th ed., *supra* note 232.

236. According to the FDA label, vincristine is indicated in acute leukemia, Hodgkin's disease, non-Hodgkin's malignant lymphomas, rhabdomyosarcoma, neuroblastoma, and Wilms' tumor. Ciprofloxacin is a widely used antibiotic.

237. CORREA, IMPLICATIONS OF DOHA, *supra* note 137, at vii, 15-16 (discussing the definition of emergency); 't Hoen, *supra* note 7, at 39-42.

238. Roger Bate, *Entire IP System Could Easily Fall*, FIN. TIMES (London), Aug. 18, 2003, at 10.

innovation is assured by high income markets alone. A few hundred thousand early AIDS cases in the United States (and government funding) were sufficient to encourage successful research programs.[239] Likewise, aggressive research programs are underway to treat most or all of the chronic conditions endemic in the high income countries. Since global disease knowledge is nonrival, it can be offered to low income populations without detriment. With innovation assured, IP law can stand aside and permit nonrival access for the poor.

Together, these implications suggest a new approach to the innovation-access conundrum, calling for a radical re-evaluation of the role of TRIPS and other laws to encourage nonrival access, with substantial potential gains in global public health.

II. THE PRAXIS OF PHARMACEUTICAL ARBITRAGE

In Part II of this Article, the theory of pharmaceutical arbitrage will be placed in two different contexts: the AIDS crisis in sub-Saharan Africa and prescription drug importation from Canada to the United States.

Certain forms of pharmaceutical arbitrage are dysfunctional—for example, diversion of differentially priced ARVs from sub-Saharan countries into high income countries. Other forms of arbitrage benefit consumers without damaging optimal innovation. The desirability of Canadian-U.S. pharmaceutical arbitrage hinges on whether global pharmaceutical rents are supra-optimal or not and whether one credits the safety of Canadian sourced drugs. If global pharmaceutical rents are supra-optimal and safety concerns properly addressed, then U.S. consumers are needlessly overcharged for patented drugs, and many unnecessarily suffer negative health outcomes from restricted access.

A. Pharmaceutical Arbitrage of AIDS Drugs in Sub-Saharan Africa

PhRMA companies have been reluctant to make patented ARV drugs available on a nonrival basis in sub-Saharan Africa. Fear of pharmaceutical arbitrage and undermining IP laws are the purported causes of this reluctance. Delayed treatment has been the proximate cause of the death of millions. Applying the theory of pharmaceutical arbitrage to AIDS may transcend the competing goals of innovation and access, by improving access while supporting optimal R&D.

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239. Indeed, many early AIDS-related drugs qualified for orphan drug status in the United States when the expected U.S. market was fewer than 200,000 persons. Salbu, *supra* note 103, at 703-07.

1. Financial Constraints Limit Access to AIDS Drugs in Sub-Saharan Africa

Globally, AIDS is not under control, with approximately forty million persons living with HIV/AIDS worldwide.[240] 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.[241] An estimated 5.5 million people in developing countries need ARV treatment for HIV/AIDS, but only five percent of those currently receive it; in sub-Saharan Africa in 2003, only one percent of the people who need ARV therapy actually receive it.[242] Large scale roll-out of ARV therapy in low income countries is now a major global public health goal.[243]

Purchasing AIDS drugs at U.S. prices is not an option for the vast majority of these people. The per capita annual cost of a popular first-line ARV in the United States is $7215,[244] and the recently introduced Fuzeon (enfuvirtide) costs $20,000 per year.[245] The annual per capita health expenditures in sub-Saharan Africa averages $29.30[246] and range from $12

240. UNAIDS/WHO, AIDS EPIDEMIC UPDATE, *supra* note 231, at 2. While much progress has been made, AIDS is not fully under control in high income countries. 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 U.S. patients have improved. *Id.* at 28-30 ("AIDS mortality continues to drop, thanks to the widespread availability of antiretroviral treatment.").

241. UNAIDS/WHO, AIDS EPIDEMIC UPDATE, *supra* note 231, at 38; Robert Greener, UNAIDS, *HIV/AIDS and Absorptive Capacity* (Kaiser Family Foundation HealthCast, Jan. 29, 2004) (2003 data) [hereinafter Greener, UNAIDS], http://www.kaisernetwork.org/health_cast/hcast_index.cfm?display=detail&hc=1066.

242. MSF, SURMOUNTING CHALLENGES, *supra* note 141, at 2, 5; *UN To Seek $6 Billion To Fight AIDS in Third World*, REUTERS, Nov. 6, 2003.

243. INST. OF MED., SCALING UP TREATMENT FOR THE GLOBAL AIDS PANDEMIC: CHALLENGES AND OPPORTUNITIES (2004); World Health Assembly, *Scaling up Treatment*, *supra* note 190.

244. Sixty tablets of Combivir cost $592.99. Drugstore.com, *at* http://www.drugstore.com (last visited Dec. 4, 2004).

245. Vanessa Fuhrmans, *Medical Dilemma: Costly New Drug for AIDS Means Some Go Without*, WALL ST. J., Jan. 13, 2004, at A1. 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 treatment. *Duke University: North Carolina Firm's New AIDS Drug Development On Hold*, U-WIRE, Jan. 22, 2004, 2004 WL 59460572 ("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*.

246. WORLD BANK, 2004 WORLD DEVELOPMENT INDICATORS (2004) (citing 2001 data).

(Malawi) to $253 (South Africa).[247] Radically reducing the price of AIDS medications for the poor is thus a necessary condition to extending ARV treatments to millions of afflicted persons worldwide.[248] Indeed, for many patients, the drugs must be free. Recognizing the important public health issues, Brazil,[249] India,[250] South Africa,[251] and China[252] produce generic ARVs for the poor, provoking conflicts between human rights and IP rights.

The European Commission has embraced voluntary "tiered [differential] pricing as the principal means of rendering essential medicines affordable . . . to the poorest populations."[253] Differential pricing is possible because of relatively low marginal costs of production. Most patented drugs can be produced relatively cheaply, absent R&D cost recovery. The primary variable expenses are direct manufacturing costs, which are a small fraction of the retail prices of patented ARVs. A high ratio of retail prices to direct manufacturing costs enables a company to sell at highly differentiated prices without selling below marginal cost.[254]

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247. *Id.*; *see also* Markus Haacker, *Providing Health Care to HIV Patients in Southern Africa, in* ECONOMICS OF ESSENTIAL MEDICINES, *supra* note 3, at 242, 244. After adjustments for purchasing power parity, Haacker's figures rise to $44.8 (Malawi) and $552.3 (South Africa).

248. Funds for ARVs and drugs to treat opportunistic infections are scarce. UNAIDS estimates these needs at approximately thirty-seven percent 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 five billion dollars. Greener, UNAIDS, *supra* note 241. If these drugs were available at a much lower cost, resources could be redeployed to prevention and other unmet priorities.

249. 't Hoen, *supra* note 7, at 32-33.

250. 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); *see also* CIPLA 2002-2003 ANNUAL REPORT, *supra* note 221, 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.").

251. Schoofs, *supra* note 250 (Indian and South African drug companies); 't Hoen, *supra* note 7, 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 PhRMA companies).

252. Jim Yardley, *China Begins Giving Free H.I.V./AIDS Drugs to the Poor*, N.Y. TIMES, Nov. 7, 2003, at A3.

253. DG TRADE, *supra* note 42, § 2.2. Low income countries targeted for essential medications by the EU had a per capita income of less than $765 in 2000.

254. SAGER & SOCOLAR, *supra* note 11, at 7 (roughly estimating marginal U.S. manufacturing and distribution costs for prescription drugs to be 9.9%).

While the public does not know the true marginal manufacturing costs of most patented drugs, differential pricing and generic production provide useful proxies.[255] Differential pricing ratios currently exceed 30:1 in ARV drugs, implying marginal costs of production in the range of 3 to 4%. For example, in November 2003, a daily dose of GlaxoSmithKline's best selling combination ARV drug Combivir[256] costs about $19.76 per day or $7215 per year by mail order in the United States.[257] In sub-Saharan Africa in 2003, GlaxoSmithKline sells Combivir to health agencies at ninety cents per day or $329 per year,[258] and has announced a new non-profit price of sixty-five cents per day.[259] Even this low price may not reflect GlaxoSmithKline's marginal cost, because Cipla sells a generic form of Combivir to governments and nonprofit agencies at thirty-three cents per day or $197.10 per year.[260] The differential pricing ratio for Combivir is

255. 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 toward 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. PhRMA simply asserts that "there is no guarantee that generic companies will price at marginal cost." Response of the Research-Based Pharmaceutical Industry to the Interim Report of the Task Force on Access to Essential Medicines, *supra* note 228, *reprinted in* DUKES, *supra* note 84, app. 2, at 27. Absent the patent monopoly, generic companies in a competitive environment will certainly price much closer to marginal cost than PhRMA companies.

256. Combivir is a fixed dose combination (FDC) of 300 mg zidovudine (ZDV or AZT) and 150 mg of lamivudine (3TC). MSF, UNTANGLING THE WEB, *supra* note 151, at 13. The best clinical FDC also adds a NNRTI. Gregory K. Robbins et al., *Comparison of Sequential Three-Drug Regimens as Initial Therapy for HIV-1 Infection*, 349 NEW ENG. J. MED. 2293 (2003); Robert W. Shafer et al., *Comparison of Four-Drug Regimens and Pairs of Sequential Three-Drug Regimens as Initial Therapy for HIV-1 Infection*, 349 NEW ENGLAND J. MED. 2304 (2003).

257. Calculation of the U.S. price comes from Drugstore.com, *at* http://www.drugstore.com (sixty tablets of Combivir for $592.99, taken twice per day) (last visited July 7, 2004).

257. 't Hoen, *supra* note 7, at 32-33.

258. MSF, UNTANGLING THE WEB, *supra* note 151, at 13.

259. GLAXOSMITHKLINE PLC, 2003 ANNUAL REPORT, Form 20-F, at 4, http://www.sec.gov/edgar/searchedgar/companysearch.html.

260. MSF, UNTANGLING THE WEB, *supra* note 151, at 15. GSK itself also issued a voluntary license to Aspen Pharmacare for production of generic Combivir. GLAXOSMITHKLINE PLC, 2003 ANNUAL REPORT, Form 20-F, *supra* note 259, at 29. Aspen's price is not yet listed in the pricing guide. MSF, UNTANGLING THE WEB, *supra* note 151, at 15.

approximately 35:1.[261] This ratio is likely to increase: MSF aims for an annual per patient cost of fifty to one hundred dollars in the near future.[262] The organization notes that achieving the lowest possible price is an urgent necessity: "If you have the option of spending $200 per person per year or $600 per person per year, and you're electing to spend $600, that means you're treating one person when you could be treating three."[263]

Triomune is Cipla's brand name for the most important triple-drug therapy fixed dose combination (FDC) for sub-Saharan Africa, containing nevirapine (NVP), stavudine (d4T), and lamivudine (3TC). Triomune is produced as a generic by Cipla Ltd. and sold for sixty-seven cents per day or US$244 per year.[264] As of July 2004, Triomune is not available in a licensed FDC form, a rare inversion in which a generic is a sole-source supplier.[265] The patents for nevirapine, stavudine, and lamivudine are held by different companies,[266] and they are apparently unable to conclude a cross-licensing agreement. Triomune's components, taken as six separate pills per day, cost about $936 per month in the United States, a ratio exceeding 46:1.[267]

High differential pricing ratios are not limited to ARVs. Ciprofloxacin is available in generic form in Africa at $0.0189 per 500 mg tablet;[268] in the U.S. retail market it sells for about five dollars a pill,[269] a ratio of 264:1. A high ratio is not necessarily a bad thing; in fact, if nonrival access is truly

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261. The numerator is $7215, and the denominator is $204.

262. MSF, SURMOUNTING CHALLENGES, *supra* note 141, 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 ORG., THE WORLD HEALTH REPORT 2004: CHANGING HISTORY 30 (2004).

263. Ellen Nakashima & David Brown, *U.S. Rule on AIDS Drugs Criticized: Ban on Using Aid To Buy Foreign Generics Hinders Treatment, Experts Say*, WASH. POST, July 14, 2004, at A12 (quoting Rachel Cohen of MSF).

264. MSF, UNTANGLING THE WEB, *supra* note 151, at 15.

265. UNICEF-UNAIDS-MSF, SOURCES AND PRICES OF SELECTED MEDICINES AND DIAGNOSTICS FOR PEOPLE LIVING WITH HIV/AIDS 18 (2004) (NVP + D4T + 3TC fixed dose combination not available in the US).

266. FDA ORANGE BOOK, *supra* note 234.

267. Epivir (lamivudine) costs about $9 per day or $270 per month; Zerit (stavudine) costs about $10.51 per day or $316 per month; Viramune (nevirapine) costs about $11.67 per day or $350 per month. All data is in U.S. dollars and is taken from http://www.drugstore.com (last visited July 8, 2004). The ratio numerator is $936, and the denominator is $20.

268. Management Sciences for Health, International Drug Price Indicator Guide, *at* http://erc.msh.org/dmpguide/ (last visited Oct. 20, 2004).

269. Drugstore.com, *at* http://www.drugstore.com (last visited July 8, 2004).

provided to the world's poorest communities, one would expect to find very large differential pricing rations.

2. IP Laws Hinder Delivery of ARVs in sub-Saharan Africa

In a widely-cited 2001 study, Attaran and Gillespie-White demonstrated the relative paucity of ARV patents in many sub-Saharan countries.[270] This article has been widely interpreted to claim that patents do not hinder ARV access in sub-Saharan Africa.[271] Attaran published a follow-on report in *Health Affairs* in 2004, again suggesting that patents have not been the major hindrance to ARV access.[272] This conclusion is not warranted from the data.

ARVs were available in the high income countries for many years before the developing world first began to receive treatment.[273] As recently

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270. Amir Attaran & Lee Gillespie-White, *Do Patents for Antiretroviral Drugs Constrain Access to AIDS Treatment in Africa?*, 286 JAMA 1186 (2001). After the manuscript was submitted, Merck gave a $25,000 grant. Several critical letters to the editor were printed in the next volume of the journal. Boelaert et al., *supra* note 141, at 840-41; Eric Goemaere et al., Letter to the Editor, 287 JAMA 841 (2002); Michael J. Selgelid & Udo Schuklenk, Letter to the Editor, 287 JAMA 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 generic production, ignoring the industrial infrastructure issue described above. Amir Attaran & Lee Gillespie-White, *In Reply*, 287 JAMA 842-43 (2002); *see also* Amir Attaran, *How Do Patents and Economic Policies Affect Access to Essential Medicines in Developing Countries?*, 23 HEALTH AFF. 155 (2004).

271. LANJOUW, INTELLECTUAL PROPERTY, *supra* note 70, at 11-12 ("[I]ndustry uses this fact [the Attaran & Gillespie-White study] to stress that patents in the poorest countries are not impeding access to drugs."); *see also, e.g.*, Harvey E. Bale, Jr., *Patents, Patients and Developing Countries: Access, Innovation and the Political Dimensions of Trade Policy*, *in* ECONOMICS OF ESSENTIAL MEDICINES, *supra* note 3, at 100, 106 n.10. Bale is the head of the international PhRMA company trade association.

272. Attaran, *supra* note 270, at 156 ("Briefly, I find that patents for essential medicines are uncommon in poor countries and cannot readily explain why access to those medicines is often lacking, suggesting that poverty, not patents, imposes the greater limitation on access.").

273. Combination therapy was available in the United States from December 1995 with

as 2002, no person in the developing world had received ARVs through official donor support from any country or multilateral institution.[274] When MSF and Partners In Health independently began ARV treatment in Thailand, South Africa, and Haiti in 2000 and 2001, some were puzzled at their attempts, due to costs per patient exceeding $10,000 to $15,000 for patented drugs.[275] Access to AIDS medications was discussed at the highest levels at the WHO as early as 1991,[276] and at the International AIDS Conference in Durban in 2000.[277] Thirteen years later, in 2004, the world is just beginning to scale-up toward universal provision of ARVs, and it is still expected to take a long time to achieve. Precious years were lost because the drugs were too expensive for the developing world, and they were too expensive because of patent protection and fears of arbitrage.[278] Millions

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the approval of the first protease inhibitors, Invirase (SQV) on December 7, 1995 and Crixivan (IDV) and Norvir (r) in early 1996. Lamivudine was approved for marketing in the United States on November 17, 1995. The U.S. Centers for Disease Control was well aware of the growing HIV/AIDS epidemic in Africa no later than the mid-1980s. RANDY SHILTS, AND THE BAND PLAYED ON: POLITICS, PEOPLE, AND THE AIDS EPIDEMIC 49, 193, 392-93, 460 (1988) ("Equatorial Africans faced death on the scale of the Holocaust.") (citing Dr. Don Francis, CDC AIDS Research, June 1984).

274. *African HIV/AIDS Crisis: Pursuing Both Treatment and Prevention: Hearing Before the Senate Comm. on Foreign Relations, Subcomm. on African Affairs*, 107th Cong. (2002) (statement of Jeffrey D. Sachs).

275. As of December 2000, the World Bank still considered ARV treatment in poor countries to be "cost-ineffective." *See* Barton Gellman, *An Unequal Calculus of Life and Death; As Millions Perished in Pandemic, Firms Debated Access to Drugs*, WASH. POST, Dec. 27, 2000, at A1 [hereinafter Gellman, *Unequal Calculus*].

276. *Id.*

277. Esther Kaplan, *Time's Up*, THE NATION, July 22, 2004, at 30, 30 ("It's been four years since the International AIDS Conference was first held in the developing world, in Durban, South Africa, where the activist demand for universal treatment access was catapulted onto the world stage. Then, the idea of treating the millions of HIV-infected people worldwide was considered farfetched. . . .The official policy of wealthy nations was to focus on prevention and leave the millions already infected to die.").

278. JOAN-RAMON BORRELL & JAYASHREE WATAL, IMPACT OF PATENTS ON ACCESS TO HIV/AIDS DRUGS IN DEVELOPING COUNTRIES (Center for Int'l Dev., Harvard Univ., CID Working Paper No. 92, 2002) (finding that a significant increase in ARV uptake would have resulted absent patents). This paper provides a static analysis which ignores the innovation question and does not model subsidized ARV markets. Had it done so, it might have demonstrated that patents have a much larger negative impact. Barton Gellman, *A Turning Point That Left Millions Behind; Drug Discounts Benefit Few While Protecting Pharmaceutical Companies' Profits*, WASH. POST, Dec. 28, 2000, at A1 ("For a decade, makers of AIDS medications had rejected the idea of lowering prices in poor countries for fear of eroding

have died, untreated, for the principle of IP law.

Attaran defends his conclusions by identifying many sub-Saharan countries wherein patents had not been filed for some ARVs. This fact is both misleading and irrelevant because the sub-Saharan countries where patents have not been filed did not possess the domestic industrial base to manufacture ARVs.[279] Throughout almost all of 2004, only one company was producing generic ARVs in Africa—South Africa's Aspen Pharmacare.[280] As one might expect, Attaran finds Aspen's home market, South Africa, to be effectively covered by patent filings.

With South Africa stymied, generic ARVs would have to be imported into sub-Saharan Africa from elsewhere, such as Brazil or India. Brazil was sued to block this practice,[281] and India has faced a U.S.-requested WTO dispute resolution on its implementation of TRIPS for pharmaceuticals,[282] as well as U.S. "Special 301" threats.[283] The USTR frequently used the Special 301 watch list to discipline countries attempting to produce generics, even if legal under domestic law or TRIPS.[284]

The mere possibility of a patent filing is likely to act as a deterrent to the filing of generic drug applications and the creation of generic manufacturing capacity in sub-Saharan Africa, since the innovator could undercut the generic company's market investment by tying them up in litigation. Unfortunately, the intended lessons of the United States's attacks on Brazil, South Africa, and India were not lost on other developing countries: All but three of Africa's least developed countries have implemented laws for pharmaceutical patents as of 2004, despite the

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profits in rich ones.").

279. CORREA, IMPLICATIONS OF DOHA, *supra* note 137, annex 2.

280. Wendell Roelf, *Aids Drugs Are Available—But Are There Enough?*, MAIL & GUARDIAN, May 17, 2004. Thembalami Pharmaceuticals in South Africa is a joint venture with Indian producer Ranbaxy, importing the APIs from India. In July 2004, Archy Pharmaceuticals Limited commissioned the creation of a pharmaceutical plant in Nigeria to produce ARVs. Godwin Haruna, *First HIV/AIDS Drug Plant Takes Off*, THIS DAY (Lagos), July 28, 2004, http://allafrica.com/stories/200407280351.html. By contrast, Asia has twenty-seven companies producing generic ARVs in eight countries. AMFAR, *supra* note 188, at 4.

281. *See supra* notes 144-145 and accompanying text.

282. World Trade Org., *India-Patent Protection for Pharmaceutical and Agricultural Chemical Products*, WT/DS50/R (Sept. 5, 1997); World Trade Org., *India-Patent Protection for Pharmaceutical and Agricultural Chemical Products*, WT/DS50/AB/R (Dec. 19, 1997).

283. U.S. OFFICE OF TRADE REPRESENTATIVE, 2004 SPECIAL 301 REPORT (2004), http://www.ustr.gov/assets/Document_Library/Reports_Publications/2004/2004_Special_301/asset_upload_file16_5995.pdf.

284. Sell, *TRIPS*, *supra* note 142, at 492.

flexibility granted by the Doha Declaration to delay implementation until 2016.[285]

Procurement policies by donors also undercut Attaran's argument. All of the AIDS/HIV drugs on the WHO Prequalification list are produced either in high income countries or in India,[286] countries now covered by TRIPS.[287] USTR and President's Emergency Plan For HIV/AIDS Relief (PEPFAR) also hinder procurement of generic ARVs by multilateral and official donors.[288]

The patent thicket effectively covers all sources of ARVs for Africa, forming an effective deterrent to ARV commercialization by generic companies, even in the absence of a formal patent filing in every sub-Saharan country. Even today, treatment with generic ARVs occurs by either complying with TRIPS flexibilities, or by (temporary) forbearance by the United States and PhRMA. Perhaps Attaran and Gillespie-White should say that patent law should not be used to delay access any longer. If so, we are in agreement. But it is historical revisionism of the foulest kind to claim that patents did not matter over the last decade for access to cheap ARV therapy in Africa.

3. Achieving Both Nonrival Access and Optimal Innovation

Next I present my proposals for maximizing public health while optimizing innovation, in light of the urgent problem of access illustrated by this case study. Nonrival access is embraced, whether through voluntary differential pricing or compulsory licensure for low and middle income markets. Dysfunctional pharmaceutical arbitrage from low income markets to high income markets is forbidden, but is not found to be a significant empirical problem. Much more troubling is the threat of counterfeit drugs. All other forms of pharmaceutical arbitrage are encouraged as a means to lower consumer prices. Finally, PEPFAR is critiqued, particularly

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285. THORPE, *supra* note 32, at 1.

286. WHO, HIV/AIDS Prequalification, 15th ed., *supra* note 232.

287. *See supra* notes 137-139 and accompanying text. As of January 1, 2005, concessions under TRIPS will be largely limited to the thirty poorest members of the WTO, excluding middle income countries such as Mexico, India, China, and Brazil. Only a few countries have notified the TRIPS Council of their intent to delay full TRIPS implementation until the January 1, 2005 deadline, namely Argentina, Cuba, India, Pakistan, Jordan, Uruguay, Egypt, United Arab Emirates, and Turkey. Indeed, all but three least developed countries in Africa have already adopted pharmaceutical patents, many years prior to the 2016 deadline. THORPE, *supra* note 32, at 1.

288. *See infra* Subsection II.A.3.iv.

for its procurement and supply chain policies which are based upon a fear of pharmaceutical arbitrage.

i. Streamline Compulsory Licensure

Compulsory licenses are difficult to administer under TRIPS. The procedures under Article 31 are time-consuming and expensive. The first two national laws implementing the Cancun General Council Decision require the grant of compulsory licenses in both the importing and exporting countries when patents have been filed.[289] The Canadian version requires a good faith effort to negotiate a voluntary license "on reasonable terms and conditions" before applying for a compulsory license, following the general language of TRIPS Article 31(b).[290] Requirements like these raise transaction costs and may allow pharmaceutical companies to delay the process for many months or years. This process is wasteful, particularly when duplicated in multiple countries.[291] Good faith negotiations are not required in two circumstances: public non-commercial use, and "national emergency or other circumstances of extreme urgency."[292] Both exceptions fit the AIDS crisis, and the former is broad enough to encompass nonrival access for global diseases.

Absent the credible threat of compulsory licensure, PhRMA companies have few economic reasons to cooperate with differential pricing, particularly for global diseases outside of the media glare of AIDS. This is not an academic exercise, as annual preventable deaths in low and middle income countries now number in the millions. The process must be simpler and faster for nonrival access to medicines.

At this time, no compulsory license has been issued under the Cancun General Council Decision (i.e., involving import or export), and only a handful of countries have issued any TRIPS-compliant compulsory licenses. Malaysia issued a compulsory license to Cipla Ltd. in February 2004 for importation.[293] As of May 2004, compulsory licenses have also been issued by Cameroon, Mozambique, and the Philippines.[294]

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289. *See, e.g.*, Norwegian Compulsory License Regulation, *supra* note 158, § 108; Canadian Bill C-9, *supra* note 158, § 21.04 (3)(d)(i)(B).

290. Canadian Bill C-9, *supra* note 158, § 21.04 (3)(c)(i).

291. Blustein & Gellman, *supra* note 150.

292. TRIPS Agreement, *supra* note 1, art. 31(b).

293. *Cipla Gets Malaysian Nod for AIDS Drugs: In a Trailblazing Move, Malaysia Has Issued a Compulsory License*, BUS. STANDARD, Feb. 26 2004, at A6.

294. Statement of the Representative of Brazil, speaking on behalf of the GRULAC countries, WHO Executive Board Meeting (May 25, 2004).

For most countries, compulsory licensing is not yet a principal mechanism for introducing generic competition and protecting public health. Many companies are engaged in cross-border sales of generic ARVs, without currently necessitating the Cancun process.[295] For example, Brazil, as permitted by its national patent laws, has been producing a number of generic ARVs for both domestic purposes and aid projects to Africa.[296] Taking another approach, Thailand simply ruled Bristol-Myers's didanosine patent invalid on public health grounds.[297]

These various tactics have led to significant generic production of at least first-line ARVs, although much of the market remains in a grey area outside of the compulsory licensing regime established by Doha. [298] A more streamlined process for compulsory licensing could bring this market in from the grey. Moreover, it could be particularly helpful with regard to second-line ARVs, where there is still inadequate availability of generics. For example, no FDC containing the second-line drug efavirenz is currently available.[299] The medical need for such second-line ARV therapy in the low and middle income countries is significant and growing. The WTO (and the USTR) should make the ARV production and export process more rational, not more difficult. A more streamlined approach to compulsory licensing would provide a well-defined mechanism that might encourage greater participation in these potential markets.

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295. Most are not prequalified by the WHO: The amfAR July 2004 report notes the difficulties with twenty-seven companies in eight countries in Asia producing generic ARVs, and only one of them (Cipla Ltd.) operating with WHO Prequalification. AMFAR, *supra* note 188, at 4.

296. Médecins sans Frontières, Brazilian Generic Drugs in South Africa—Background (Jan. 29, 2002), *at* http://www.msf.org/countries/page.cfm?articleid=F8557436-9B60-4D00-BC5F0476D8B7A5E1.

297. Gov't Pharm. Org. v. Bristol-Myers, Thailand Central Intellectual Property Court, Oct. 2002.

298. MSF, UNTANGLING THE WEB, *supra* note 151, at 5-7.

299. *Id.* at 6. This may be because of pressures applied to potential source countries—such as India and Thailand—by the USTR under the Special 301 process. U.S. TRADE REP., 2004 NATIONAL TRADE ESTIMATE REPORT ON FOREIGN TRADE BARRIERS, 217-220 (2004) (India); *id.* at 463-65 (Thailand). The United States and Thailand are negotiating a free trade agreement with TRIPS-plus provisions. *See* Thai Free Trade Agreement Watch Website, *at* http://www.ftawatch.org (last visited Sept. 2003); *see also* Marwaan Macan-Markar, *Thailand-U.S.: Freer Trade Weakens Access to HIV/AIDS Drugs*, INTER PRESS SERVICE NEWS AGENCY, May 21, 2004, http://www.ipsnews.net/africa/interna.asp?idnews=23849. Fortunately, despite trade-related pressures, Thailand is now preparing a generic FDC as a second-line therapy, containing efavirenz, lopinavir and ritonavir.

ii. Dysfunctional Pharmaceutical Arbitrage of AIDS Drugs

a. Dysfunctional Arbitrage Is Rarely Observed

International arbitrage certainly seems to pose a plausible risk to pharmaceutical companies. The consumer retail price of a kilogram of the active ingredients in Combivir[300] is about $20,000 in the United States, but sells for as little as $612 in Hyderabad and sub-Saharan Africa.[301] This price differential is equal to about twenty-five times the average per capita income in the lowest income countries. Neo-classical economic theory predicts that entrepreneurs[302] will divert these drugs from the poor and export them to wealthy countries where they will fetch higher prices. Domestic arbitrage occurs within the United States at much lower thresholds.[303] Since the great majority of the world's AIDS patients are in poorer countries, if only a small percentage were diverted, significant volumes of ARVs could flow into high income country markets.[304]

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300. Combivir is GlaxoSmithKline's best selling ARV drug, and the company holds a forty-five percent global market share in HIV/AIDS drugs. *See* 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; GLAXOSMITHKLINE PLC, 2003 ANNUAL REPORT, Form 20-F, at 63, http://www.sec.gov/edgar/searchedgar/companysearch.html (total of all HIV sales).

301. The active ingredients in Combivir total 450 mg per tablet. A kilogram of active ingredients will create approximately 2222 tablets. The retail price of 2222 tablets of Combivir in the U.S. retail market exceeds $20,000. *See* Drugstore.com, *at* http://www.drugstore.com (last visited July 9, 2004).

302. Or smugglers, depending upon your perspective.

303. *See infra* Subsection II.B.2. Jackie Judd, Senior Fellow with the Kaiser Family Foundation, Interview with Gilbert M. Gaul and Mary Pat Flaherty, Interview with *Washington Post* Reporters on Drug Safety Articles (Oct. 24, 2003), http://www.kaisernetwork.org/health_cast/hcast_index.cfm?display=detail&hc=1004 (describing significant arbitrage diversion within the U.S. market taking advantage of relatively modest price differentials).

304. The United States is a likely target market. The EU may not be as vulnerable to diversion because most of its citizens are covered by a third party prescription drug benefit and are not as price sensitive. DG TRADE, *supra* note 42, § 3.3. This conclusion might be true for ultimate consumers, but European intermediaries such as parallel traders could seek arbitrage earnings from this trade. The available evidence suggests that European parallel traders are closely scrutinized and do not knowingly participate in illegal diversions. *See, e.g.*, Glaxo Group Ltd. v. Dowelhurst Ltd., [2004] E.T.M.R. 39 (July 31, 2003), 2003 WL 21729286.

Further, criminal organizations might be attracted to the profits to be found in dysfunctional pharmaceutical arbitrage. The pricing ratios operating in the illegal cocaine market are broadly similar to ARV pricing ratios. The U.S. wholesale price of a kilogram of cocaine ranges from $13,000 to $25,000,[305] comparable to the U.S. retail value of a kilogram of the active ingredients in Combivir.[306] The U.S. retail price of a gram of cocaine is about $100.[307] The retail price of cocaine in Columbia is between three dollars and five dollars per gram,[308] yielding a ratio of about 25:1.[309] Since ARV arbitrage offers potentially higher profits than cocaine trafficking, one might expect criminal enterprises to enter the ARV business, especially since the risk of apprehension and punishment are so severe for cocaine trafficking, but relatively modest for prescription drug counterfeiting.[310]

Given these facts, it would be striking if dysfunctional ARV arbitrage did not occur. And yet reality appears to depart from the neo-classical economic model, for there is quite limited evidence of dysfunctional arbitrage. It is notable that generic drugs have been produced in India for decades without apparently infiltrating or undermining Western markets.[311] As of April 2002, both the European Commission and the pharmaceutical companies acknowledged that pharmaceutical arbitrage from poor countries into high income countries was "still largely theoretical."[312] Only

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305. U.S. DRUG ENFORCEMENT ADMIN., DRUG TRAFFICKING IN THE UNITED STATES (2001), http://www.usdoj.gov/dea/pubs/intel/01020/index.html (2000 data). Retail prices per gram are significantly higher, particularly for smaller quantities.

306. *See supra* note 301.

307. OFFICE OF NATIONAL DRUG CONTROL POLICY, TRENDS IN COCAINE PRICES (1981-2000) (price per gram for purchase of one to ten grams). The UK price for a gram in similar lots is around £50. Independent Drug Monitoring Unit Ltd., UK Drug Prices 2002, http://www.idmu.co.uk/prices02.htm.

308. This figure is from a hopelessly anecdotal source, a travel journal of an American using drugs in Columbia. David Ashley, Cocaine in Columbia (June 14, 2000), *at* http://www.erowid.org/experiences/exp.php?ID=1796 (last visited Oct. 20, 2004).

309. The numerator is $100 per gram and the denominator is $4 per gram.

310. ALLIANCE AGAINST COUNTERFEITING & PIRACY, PROVING THE CONNECTION: LINKS BETWEEN INTELLECTUAL PROPERTY THEFT AND ORGANISED CRIME 7-8 (2002), http://www.a-cg.com/index2.html (last visited Oct. 20, 2004).

311. One would expect that over the past twenty years there would have been some significant reported court cases on illegal imports of Indian and other unlicensed generics if the problem were widespread. Andrew Farlow of Oxford finds little evidence of diversion. Andrew Farlow, Costs of Monopoly Pricing Under Patent Protection, Presentation at Columbia University slide 19 (Dec. 4, 2003).

312. DG TRADE, *supra* note 42, at § 3.3.

six months later, GlaxoSmithKline, the patent holder for several important AIDS drugs, brought the sensational charge that 36,000 packages of HIV/AIDS medicines worth approximately US$18 million were found to have been diverted from West Africa to the EU.[313] GlaxoSmithKline sued several participants in the transactions, including a legal parallel trader in pharmaceuticals, Dowelhurst Ltd, for trademark infringement.[314]

The Dowelhurst case unearthed several remarkable facts which undercut the public relations spin that Glaxo had put on the case. First, ninety-nine percent of the packages handled by Dowelhurst were not part of Glaxo's charitable access initiative for Africa, but were ordinary commercial sales to Africa, at prices approximating EU prices.[315] The Deputy Judge expressed keen displeasure upon finally understanding this point, as he had been led to believe that all of the packages were destined for charitable access programs.[316] Second, 99% of the packages had been sold within Europe, to addresses in France, and probably never made the trip to Africa.[317] The alleged diversions occurred in Europe, not in Africa. I say alleged diversions, because the case makes clear that the resale of the drugs was not proscribed by contract.[318] Third, by placing the packages into commerce within Europe, Glaxo exhausted its IP rights within Europe.[319] Finally, Glaxo sold the packages without any attempt to label them as ineligible for sale or reimportation into the EU. They were packaged in French, with EMEA license codes and nothing was done to indicate they

313. There were a number of media reports from three continents in October 2002. *See, e.g.*, Sarah Boseley & Rory Carroll, *Profiteers Resell Africa's Cheap Aids Drugs*, THE GUARDIAN, Oct. 4, 2002, at P1; *see also* DUKES, *supra* note 84, at 50 & n.1.

314. Glaxo Group Ltd v. Dowelhurst Ltd, [2004] E.T.M.R. 39 (July 31, 2003), 2003 WL 21729286.

315. *Id.* ¶ 36.

316. *Id.* ¶ 46. The Deputy Judge imposed over ninety percent of the litigation costs on Glaxo, in part because he felt misled. Glaxo Group Ltd. v. Dowelhurst Ltd., [2003] E.W.H.C. 3060 (High Ct., Ch. Div. 2003), ¶¶ 10, 17.

317. Glaxo Group Ltd. v. Dowelhurst Ltd., [2004] E.T.M.R. 39 (2003), ¶¶ 66-76. Only one percent of the packages had actually been sold to a buyer in Africa, namely the packages involved in the access program.

318. *Id.* ¶ 39.

319. *Id.* ¶¶ 66-76. On appeal, the Court of Appeal upheld the Deputy Judge's rulings on summary judgment, permitting the trial to proceed on the question of compliance with EU rules for pharmaceutical parallel trade. Glaxo Group Ltd. v. Dowelhurst Ltd., [2004] E.W.C.A. Civ. 290 (App. Ct., Civ. Div., 2004). Specifically, the Court of Appeals upheld the exhaustion rule on 100% of the packages rather than just 99%. *Id.* ¶¶ 30-40.

were destined for a charitable access program.[320] Legal European parallel traders were led to believe the drugs had been lawfully placed into European commerce. Indeed, the defendant suggested that Glaxo did so deliberately in order to generate the resulting publicity.[321] Within three weeks of the Glaxo diversion story, the European Commission announced plans to issue a regulation to curb such diversions.[322] The 2003 Council Regulation promptly required many modifications to packages and pills destined for essential access programs.[323]

The only other major media report of diversion of essential access drugs was in Forbes in April 2004, noting allegations of diversion in Indonesia, Chile, and Lebanon.[324] This story parroted PhRMA's spin on the 2002 Glaxo case in Europe, but failed to mention any of the facts from the Dowelhurst case discussed above. The source of the report in Indonesia was a survey in Jakarta by a respected local health group, which found many donated drugs being either sold on the black market in Jakarta or available in the public health clinics for a price in excess of the statutory maximum.[325] This is a simple case of local corruption, and there is no evidence that the drugs were leaving the immediate market. This situation might be regrettable, but it is not dysfunctional arbitrage; it does not replace commercial markets in the high income countries. Similar local diversions occur in the United States.[326] The reports from Chile and Lebanon are sourced exclusively from local affiliates of PhRMA. Neither report was substantiated; nor do they suggest dysfunctional arbitrage as opposed to local movement of drugs within low or medium income countries. In sum, empirical evidence to date does not indicate a sizable

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320. *Glaxo Group Ltd*, [2004] E.T.M.R. at ¶¶ 46-50.

321. *Id.* ¶¶ 51-53.

322. *EU/WTO – Plan to Curb Illicit Medicines Trade*, EUR. REP., Oct. 26, 2002.

323. At present, the European Union Council Regulation only applies to "tiered price" pharmaceutical exports to seventy-six listed developing and least-developed countries and to "HIV/AIDS, malaria, tuberculosis and related opportunistic diseases" (a limitation which should be amended following Cancun). The European Union defines a "tiered price" pharmaceutical as being offered to the poor for either direct manufacturing cost plus no more than fifteen percent or at less than twenty-five percent 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. (L 135/6) art. 3(a) [hereinafter Council Regulation 953/2003].

324. Richard C. Morais, *"Pssst . . . Wanna Buy Some Augmentin?,"* FORBES 2000, Apr. 12, 2004, http://forbes.com/forbes/2004/0412/112_print.html.

325. *Id.*

326. Judd, *supra* note 303.

arbitrage market in ARVs from low income countries into the high income countries.

b. Measures To Hinder Dysfunctional Arbitrage

Possible reasons for the dearth of empirical evidence of dysfunctional pharmaceutical arbitrage include moral and legal sanctions within high income market countries. The impact of these norms is significant in pharmaceutical arbitrage markets. When pharmaceutical arbitrage is unmistakably legal, it flourishes, even at low differential pricing ratios. For example, the EU follows the "community exhaustion" rule, permitting parallel trade in patented and trademarked products within the European Economic Area. Differential pricing ratios of less than 2:1 have been sufficient to create a multi-billion euro legal arbitrage market within the EU,[327] subject to complex rules on repackaging and trademark infringement devised by the European Commission and the European Court of Justice.[328] In the European Union, illegal pharmaceutical arbitrage is rarely observed.[329]

Canada provides a contrasting example. Pharmaceutical arbitrage from Canada to the United States operated for years under legal ambiguity. Proponents touted the enhanced consumer access. The pricing differential is less than 2:1, but the arbitrage market now is in the range of $600 million to $1.1 billion a year.[330]

So the first imperative is to prevent any legal or moral uncertainty concerning dysfunctional arbitrage. At a minimum, diversion of drugs intended for the poor to high income country markets should be clearly illegal. The European Union, for example, promptly moved in this direction following media reports of the Glaxo diversion.[331] The United States should follow suit.

The second task is to modify the product to resist substitutability. The

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327. PETER WEST & JAMES MAHON, BENEFITS TO PAYERS AND PATIENTS FROM PARALLEL TRADE (York Health Econ. Consortium, Working Paper, 2003) (estimating direct savings of 631 million in 2002 from legal pharmaceutical arbitrage (parallel trade) within the EU) (funded by a grant from European parallel traders). *But see* KANAVOS ET AL., *supra* note 54, at 15-16 (finding meager benefits to consumers from parallel pharmaceutical trade) (funded by an unrestricted grant from Johnson & Johnson).

328. For a recent discussion, see Boehringer Ingelheim KG v. Swingward Ltd., [2004] E.T.M.R. 65 (2004), 2004 WL 343819, at ¶¶ 3-17.

329. *See supra* Subsection II.A.1.

330. *See infra* Subsection II.B.2.

331. *See* Council Regulation 953/2003, *supra* note 323, art. 7.

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 General Council Decision addresses this issue: Exporting countries must clearly identify the products through labeling or marking and through special coloring or shaping.[332] The EU Council Regulation follows this tact.[333] GlaxoSmithKline and others are complying, altering both the packaging and the color of the product.[334] These steps will eliminate the flow of improperly diverted essential access medicines through legal distribution channels such as parallel traders and distribution companies.

Third, the manufacturer also has the responsibility to deliver the essential medicines to a reputable supply chain located outside of the United States or European Union, in order to avoid domestic exhaustion.

Fourth, consumers in high income markets 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 should not be an implicit safety warning that "those pills may not be safe," since Africans will be told exactly the opposite: "The red pills are safe and effective."[335] Advertising should describe diversion as a moral and legal issue: High income patients who take pills intended for impoverished Africans are stealing from the poor.[336] Under the European Union Council Regulation, all covered pharmaceuticals exported from the European Union will bear a special logo identifying the product as destined for the poor.[337] In addition, domestic law within the high income countries should criminalize the practice.

The final front for anti-diversion measures is the borders of the high income countries. Pharmaceutical arbitrage may become dysfunctional

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332. *Cancun General Council Decision, supra* note 137, ¶ 2(b).

333. *See* Council Regulation 953/2003, *supra* note 323, art. 7, ¶ 10. While the Council Regulation addresses importation in luggage for personal use, similar to the U.S. personal importation rule, it does not address (but probably covers) Internet sales. *Id.* art.10, ¶ 13,. Seized product may be used for humanitarian purposes. *Id.* ¶14.

334. GLAXOSMITHKLINE PLC, 2003 ANNUAL REPORT, Form 20-F, at 29.

335. Vertical product differentiation based on quality is common in some products (regular versus premium gasoline), but is probably untenable in pharmaceuticals.

336. If the arbitraged drugs were voluntarily sold rather than stolen, then the moral claim weakens.

337. Council Regulation 953/2003, *supra* note 323, 2003 O.J at art. 7. The logo is found in Annex V of the regulation.

only when diversion occurs from low or middle income markets to high income markets. Trade among or between low and middle income markets is not dysfunctional.[338] Thus, the key moment to control dysfunctional arbitrage is at the border of high income countries, not at the border of the exporting country. These protections can be put into place immediately by high income countries and do not depend upon reaching a multilateral agreement at the WTO. Furthermore, the high income countries possess the resources and infrastructure to make interdiction a reality. Indeed, the absence of observed dysfunctional arbitrage may well be a result of the border controls over the entry of drugs that many high income countries enjoy.

c. Low and Middle Income Markets Should Not Bear the Burden of Anti-Diversion Measures

The most striking aspect of these anti-diversion measures is that the responsibility for all of them logically rests upon the manufacturers and high income markets. None of the five measures require expenditure by low or medium income countries. Nevertheless, when PhRMA companies finally agreed to significant differential pricing of ARVs in low income countries, they insisted on strong anti-diversion protections and burden-sharing by the recipient countries.[339] The Cancun General Council Decision 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."[340] Under Cancun, developing and least developed countries inappropriately bear these costs even if global pharmaceutical rents are supra-optimal.[341]

Minor diversions at the clinic or patient level should not be an international enforcement focus. Given the difficulty in setting up a source collection system, it is unlikely that small batches or individual blister packs without packaging will filter back to high income country markets in significant quantities. Minor local diversions are likely to remain in the region and may well be re-sold to other poor patients outside of the

338. *See supra* Subsection II.A.2.iii.

339. Gellman, *supra* note 150.

340. *Cancun General Council Decision, supra* note 137, ¶ 4.

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

current distribution system.[342] This is not a best-case result, but preventing this arbitrage is not an enforcement priority. The priority should be to address weaknesses in the supply chain that allow large batches to be diverted in a single transaction. The risk may be greatest while the product is still outside of the recipient country.[343]

Finally, the heuristic suggests that some level of dysfunctional arbitrage may be tolerable from an innovation point of view. So long as commercial markets are not replaced, the practice will not harm innovation. Modest leakage from commercial markets may reduce rents, but will not harm innovation if overall rents remains supra-optimal.

iii. Counterfeit Drugs

In the debates over essential medicines, care must be taken to distinguish arbitrage from counterfeiting. The term "counterfeit" is often loosely applied in a manner which conflates several categories of products:[344] safe and effective drugs that have entered the United States improperly, drugs that are intended to be legitimate but are "sub-standard" in some way, and those that are blatant attempts to defraud consumers by selling fake drugs.[345] While all these types of products may raise concerns for consumers,[346] I focus my analysis here on the third, narrow category—

342. This appears to be the case in Jakarta. *See generally* Morais, *supra* note 324.

343. Both conditions were present in the Glaxo case.

344. *See Prescription for Danger: Counterfeit Drug Trade Grows*, CBSNEWS.COM, Aug. 2, 2001, *at* http://www.cbsnews.com/stories/2002/01/31/health/main327265.shtml ("There is no single definition for counterfeit drugs. The may contain dangerous substitutes instead of the real ingredients. Or they may be much like 'the real thing'—only expired, or not approved for sale in the [United States].").

345. For discussion of the FDA's definition, see *Examining the Implications of Drug Importation: Hearing Before the Senate Judiciary Comm.*, 108th Cong. (2004) (statement of William K. Hubbard, U.S. FDA Associate Commissioner for Policy and Planning), http://www.fda.gov/ola/2004/importeddrugs0714.html. *See also* Heather Won Tesoriero, *Fake-Drug Sites Keep a Step Ahead*, WALL ST. J., Aug. 10, 2004, at D4 (describing generic versions which were substituted for brand name drugs still patented in the United States as "counterfeits"); *Options for Safe and Effective Prescription Drug Importation: Hearing Before the Senate Comm. on Commerce, Science, & Transportation*, 108th Cong. (2004) (statement of Mark McClellan, Commissioner of the FDA), http://commerce.senate.gov/hearings/testimony.cfm?id=1105&wit_id=3132 (discussing "unapproved, imported pharmaceuticals" and "unsafe and illegal drugs" along with "ineffective, counterfeit" drugs).

346. *See* FDA, COUNTERFEIT DRUG TASK FORCE INTERIM REPORT 5-7 (2003), http://www.fda.gov/oc/initiatives/counterfeit/report/interim_report.html (noting that counterfeit drugs may "pose significant public health and safety concerns," as they "may

products which do not contain the proper active ingredient (for example, where the counterfeit is essentially a placebo product). These "non-functional" counterfeits merit special consideration because of the particular incentives for, and dangers of, their production.[347]

Empirical evidence suggests that virtually none of the internationally arbitraged drugs arriving in the United States are non-functional counterfeits; their importation is most likely to simply violate technical restrictions on parallel importation, FDA approval or labeling, or other laws.[348] Instead, most of the blatantly fake or nonfunctional counterfeit drugs in the United States have domestic origins or domestic networks.[349] While the FDA still considers it a relatively rare practice,[350] it is nevertheless growing rapidly in the United States and in other high income markets.[351] In 2000, the estimated value of EU pharmaceutical counterfeiting was

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contain only inactive ingredients, incorrect ingredients, improper dosages, sub-potent or super-potent ingredients, or be contaminated."); EUROPEAN FED'N OF PHARM. INDUS. & ASS'NS, INTERNATIONAL EXHAUSTION OF TRADE MARK RIGHTS 7 (2001) (describing the range of products that may be considered counterfeit by the WHO and the European pharmaceutical trade association and corresponding concerns).

347. My point is not to argue whose definition is "right," but to demonstrate the analysis which is possible when focusing on this narrower category. In copyright and trademark practice, a "counterfeit" or "pirated" copy is one that was manufactured by an unlicensed source, but such copies are likely to be as functional as the genuine article: A counterfeit Gucci purse might nevertheless be a fully functional and stylish purse. In pharmaceuticals, non-functional counterfeits are, arguably, particularly likely. *See infra* note 353 and accompanying text.

348. *See, e.g.*, Press Release, FDA, Recent FDA/U.S. Customs Import Blitz Exams Continue To Reveal Potentially Dangerous Illegally Imported Drug Shipments (Jan. 27, 2004) (mentioning many categories of unapproved drugs but never indicating that any of them contained no active ingredient).

349. Gilbert M. Gaul & Mary Pat Flaherty, *U.S. Prescription Drug System Under Attack: Multibillion-Dollar Shadow Market Is Growing Stronger*, WASH. POST, Oct. 19, 2003, at A1.

350. FDA, *supra* note 346, at 3.

351. The FDA estimates that pharmaceutical counterfeiting has increased four-fold in the past few years. *See, e.g.*, Mary Pat Flaherty & Gilbert M. Gaul, *Anti-Counterfeit Steps Drugmakers Sought; Legislators' Goal Is To Halt Illegal Sales*, WASH. POST, Jan. 17, 2004, at A11; Mary Pat Flaherty & Gilbert M. Gaul, *Miami Man Charged with Selling Counterfeit Lipitor*, WASH. POST, Dec. 6, 2003, at E1; Mary Pat Flaherty & Gilbert M. Gaul, *Lax System Allows Criminals To Invade the Supply Chain*, WASH. POST, Oct. 22, 2003, at A1. These articles were part of a series of articles on counterfeit drugs by Mary Pat Flaherty and Gilbert M. Gaul that ran in the *Washington Post* during Fall 2003/Winter 2004. The *Wall Street Journal* has also covered the story. *E.g.*, Anna Wilde Mathews & Heather Won Tesoriero, *Murky Channels: Bogus Medicines Put Spotlight on World of Drug Distributors*, WALL ST. J., Sept. 29, 2003, at A1.

more than 1.5 billion Euros. The United Kingdom-based Anti-Counterfeiting Group estimated in 2003 that 5.8% of pharmaceutical company annual revenue is lost due to counterfeiting.[352] If true, counterfeiting is a major threat not only to public health, but also to innovation, far outstripping the limited potential damage from dysfunctional pharmaceutical arbitrage.

Criminal enterprises are currently involved in pharmaceutical counterfeiting.[353] Counterfeiting opportunities may explain the absence of criminal ARV arbitrage. In the illegal, nonprescription drug market, counterfeiting is a difficult practice: If users do not get high, the product will not sell, particularly in sales between repeat players. In prescription drugs, however, the opportunity for counterfeiting is much greater. Patients are often unable to tell whether a counterfeit pill contains the correct active ingredients. It may take weeks or months to notice that therapy is failing, and the cause of failure may not be linked with the counterfeits. Counterfeits may be introduced into legitimate supply chains, diluting therapy while making the counterfeiting more difficult to observe and trace. These information characteristics enable the criminal seller of counterfeit prescription drugs to act as if the transactions were discrete, rather than repeating.

While obtaining arbitraged ARVs might be possible, obtaining them in sufficient quantities would require a procurement team in the field (e.g., sub-Saharan Africa), with multiple diversions against alerted supply chains, followed by repackaging and illegal reverse supply chains back to high income country markets. Counterfeiting is arguably easier than diverting pills from Africa: Drugs labeled and packaged to look like the authentic licensed product (rather than distinguishable pills in packaging labeled for essential medicine programs) can be introduced into high income country supply chains directly. Counterfeiting dispenses with many costs. The per-pill cost to produce a placebo without active ingredients may be far cheaper than covert diversion and procurement, re-coloration, repackaging, and transportation. Finally, it is unlikely that anyone would bother to counterfeit a cheap generic drug. Expensive, patented drugs are the targets of counterfeiters; cheap generics are not.[354] A criminal is

352. THE ANTI-COUNTERFEITING GROUP, WHY YOU SHOULD CARE ABOUT COUNTERFEITING 14, http://www.a-cg.com/docs/why_you_should_care.pdf (last modified June 22, 2004).

353. ALLIANCE AGAINST COUNTERFEITING & PIRACY, *supra* note 310, at 2 ("This document provides clear and unambiguous evidence of organised crime controlling, exploiting and benefiting from intellectual property fraud. It is on the increase.").

354. The examples of counterfeits in most media and FDA reports are of expensive

unlikely to counterfeit a pill and sell it as aspirin or Triomune, when it could be sold as Lipitor or Fuzeon. When low-cost generics are available on a nonrival basis, the threat of counterfeits recedes.

Counterfeits, not dysfunctional arbitrage, are the more immanent danger to both public health and PhRMA innovation. Counterfeiting will remain an issue so long as the actual product has a high value relative to the cost of manufacturing a plausible placebo. Taking all R&D cost recovery out of the price system will greatly reduce counterfeiting pressure, but so long as a placebo can be made for a fraction of the value of the actual pill, counterfeiting will remain an issue. The Hubbard-Love R&D Treaty thus would wipe out much of the current incentives to counterfeit, by removing R&D cost recovery from the retail sales price.[355] Likewise, nonrival access in low and middle income countries would create the same conditions.

Additional anti-counterfeit measures in high income countries should include a pedigree system of tracing drugs from the manufacturer to the consumer. A pedigree system (or the European system of parallel traders giving notice of intent to trade) would also hinder arbitrage by making product movement transparent to the manufacturer. Most importantly, routine market sampling for counterfeits must be introduced, and sources of counterfeit drugs aggressively traced by law enforcement.[356]

iv. Implications for PEPFAR

When the Bush Administration established PEPFAR, it chose to largely bypass existing multilateral institutions such as the Global Fund. PEPFAR calls for only 6.3% of the $15 billion to be placed with the Global Fund, with the remainder devoted to unilateral U.S. efforts.[357] This move reflects the Bush Administration's penchant for unilateralism, even in the world of AIDS.

The Global Fund's procurement and supply management guidelines prioritize lowest price, assured quality, and legal compliance.[358] Grant

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patented drugs such as Lipitor, Epogen, Zyprexa, and Serostim. *See* Leila Abboud et al., *Fakes in the Medicine Chest; As Drug Counterfeiting Rises, FDA May Propose Changes in Sales, Distribution Network*, WALL ST. J., Sept. 22, 2003, at B1.

355. *See supra* note 213 and accompanying text.

356. Some steps towards an anti-counterfeiting policy are being taken by the FDA. FDA, *supra* note 346, at 18-22.

357. THE PRESIDENT'S EMERGENCY PLAN FOR AIDS RELIEF: U.S. FIVE-YEAR GLOBAL HIV/AIDS STRATEGY 16 (2004).

358. THE GLOBAL FUND TO FIGHT AIDS, TUBERCULOSIS, & MALARIA, GUIDE TO THE GLOBAL

recipients retain flexibility in how they balance cost, quality, and access in the local context. For example, a recipient country could choose to rely on the WHO prequalification process as the quality mechanism on ARV drugs, or it could choose to impose different standards based on local collective preferences. Similar choices may be made between branded drugs and generics.

One way to understand PEPFAR is that it inverts the Global Fund's ARV procurement priorities and strikes a different balance between access and innovation. PEPFAR gives first priority to legal compliance (and highest quality) rather than lowest effective cost, shunning generics.[359] PEPFAR requires approval by a "stringent regulatory authority" before procurement, meaning the NDRAs from the United States, EU, and Japan (the ICH), and possibly Canada.[360] Critics attacked these standards as inappropriate barriers to rapid roll-out. On May 16, 2004 PEPFAR announced a new "fast track" FDA certification for generic ARVs, rather than following the WHO pre-certification process.[361] PEPFAR will impose "all FDA standards for drug safety, efficacy, and quality,"[362] even though existing studies have proven the efficacy of ARV treatment with generics.[363]

FUND'S POLICIES ON PROCUREMENT AND SUPPLY MANAGEMENT (2004), http://www.theglobalfund.org/pdf/guidelines/pp_guidelines_procurement_supplymanagement_en.pdf.

359. From the beginning, PEPFAR guidance to its field offices prohibited acquisition of cheaper generic FDCs. U.S. GEN. ACCOUNTING OFFICE, GAO-04-784, U.S. AIDS COORDINATOR ADDRESSING SOME KEY CHALLENGES TO EXPANDING TREATMENT, BUT OTHERS REMAIN 37 (2004). A cynic might view "highest quality" as merely a stalking horse for "highest price."

360. *Id.* at 19-37.

361. Tommy G. Thompson & Randall L. Tobias, HHS Proposes Rapid Process of Fixed Dose Combination and Co-Packaged Products: Joint Statement Issued by HHS Secretary Thompson and U.S. Global AIDS Coordinator Tobias (May 16, 2004), http://www.state.gov/r/pa/prs/ps/2004/32503.htm; *see also* Gautam Naik et al., *Viral Strain: In AIDS Fight, Ambitious Goals Meet Hard Realities - Millions of Ill in Poor Nations Fail To Get Drugs as Funds, Medical Systems Fall Short*, WALL ST. J., July 1, 2004, at A1; 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 D5 (raising unresolved questions about whether the Office of the U.S. Global AIDS Coordinator will procure generic AIDS drugs at the lowest possible price).

362. *HIV/AIDS Fiscal Year 2005 Budget Request: Hearing of the Subcomm. on Foreign Operations of the Comm. on Appropriations*, 108th Cong. (2004) (statement of Randall L. Tobias, U.S. Global AIDS Coordinator), http://appropriations.senate.gov/hearmarkups/record.cfm?id=221702.

363. S. PUJARI ET AL., SAFETY AND LONG-TERM EFFECTIVENESS OF GENERIC FIXED-DOSE FORMULATIONS OF NEVIRAPINE-BASED HAART AMONGST ANTIRETROVIRAL-NAÏVE HIV-INFECTED PATIENTS IN INDIA (2003) (background document for WHO meeting on Fixed Dose

PEPFAR is also creating its own supply chain management system, independent of The Global Fund.[364] These efforts are duplicative and will inevitably raise costs and delay treatment.[365] Amazingly, the United States funds both programs and remains the largest donor to The Global Fund.[366]

Three aspects of PEPFAR are worthy of detailed discussion. PEPFAR erects hurdles to procurement of generic ARVs in order to steer additional volume at higher prices to PhRMA companies. It establishes a separate supply chain, permitting the United States to maximize protection against diversion and arbitrage.[367] And, finally, it controls quality hoping to delay the onset of resistance. My recommendations to PEPFAR's administrators are as follows:

a. Purchase Generics

The first goal is not legitimate on innovation grounds, since donor programs do not replace existing commercial markets for ARVs. PEPFAR's unilateralism is not needed for innovation, but imposes American notions of the appropriate quality-access balance upon desperately poor countries. Innovation does not require ignoring their collective preferences for low cost treatment under WHO prequalification. PEPFAR appears to operate in the mode of many bilateral aid projects, as a subsidy for domestic exports. The PEPFAR legislation requires fifty-five percent of the U.S. contribution to be used in treatment, and seventy-five percent of that amount (or 41.25% of the total) to be spent on ARVs for fiscal years 2006 through 2008.[368] Blocking generic ARVs will funnel $6.18 billion dollars in

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Combinations for HIV/AIDS, Tuberculosis, and Malaria); Christian Laurent et al., *Effectiveness and Safety of a Generic Fixed-Dose Combination of Nevirapine, Stavudine, and Lamivudine in HIV-1-Infected Adults in Cameroon: Open-Label Multicentre Trial*, 364 THE LANCET 29 (2004); Gregory K. Robbins et al., *Comparison of Sequential Three-Drug Regimens as Initial Therapy for HIV-1 Infection*, 349 NEW ENG. J. MED. 2293 (2003); Robert W. Shafer et al., *Comparison of Four-Drug Regimens and Pairs of Sequential Three-Drug Regimens as Initial Therapy for HIV-1 Infection*, 349 NEW ENG. J. MED. 2304 (2003).

364. U.S. AGENCY FOR INT'L DEV., DRAFT STATEMENT OF WORK PUBLISHED FOR COMMENT—SUPPLY CHAIN MANAGEMENT SYSTEM FOR THE PRESIDENT'S EMERGENCY PLAN FOR AIDS RELIEF (2004).

365. *See, e.g.*, U.S. GEN. ACCOUNTING OFFICE, *supra* note 359; Mark Schoofs, *At Zimbabwe Clinic, Wait Is Long and U.S. Drug Cupboard Is Bare*, WALL ST. J., July 1, 2004, at A8.

366. *See* THE GLOBAL FUND TO FIGHT AIDS, TUBERCULOSIS & MALARIA, ANNUAL REPORT 2003 (2003).

367. U.S. AGENCY FOR INT'L DEV., *supra* note 364, at 6.

368. United States Leadership Against HIV/AIDS, Tuberculosis, and Malaria Act of 2003,

additional ARV sales to PhRMA companies,[369] at a price much higher than generics.[370] PEPFAR's stand also diverts those unit sales away from companies such as Cipla, another move advantageous to PhRMA companies.

b. Do Not Create Duplicate Supply Chains

The heuristic tells us that the second goal may be legitimate: Avoid arbitrage from donor programs to high-income markets. But the analysis is not so simplistic. PEPFAR costs are very significant, including both duplicated program expenses and indirect costs from delayed and constrained treatment. PEPFAR is devoting special multi-billion dollar efforts to minimize drug diversion within the recipient countries.[371] These costs should be balanced against the benefits of averted arbitrage. Most arbitrage is not harmful to innovation, and modest levels of dysfunctional arbitrage may be tolerable, particularly in conditions of supra-optimality.[372]

c. Generic FDCs Delay Resistance

PEPFAR's final goal is quality, together with the fear of mismanagement, leading to resistance. This is an important question. Unfortunately, it is likely that another parallel AIDS relief system will hinder the uniform management of the disease. A parallel system further complicates treatment in the field and confuses providers. Resistance must be managed globally. Furthermore, if PEPFAR's primary goal is the avoidance of resistance, it should not erect barriers to Triomune and other FDCs, which are the first-line treatments most effective in preventing the emergence of resistant strains, but which are only available as generic in FDC form. PEPFAR's insistence on U.S. FDA standards will delay the procurement of FDCs. If PEPFAR requires the same standards on anti-malarial FDCs (Fixed-done Artesunate Combination Therapy or FACT), the most effective treatment for managing malarial resistance will be unnecessarily delayed,[373] despite the fact that WHO has already

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Pub. L. No. 108-25, § 403 (2003), 117 Stat. 711.

369. 41.25% of $15 billion.

370. U.S. GEN. ACCOUNTING OFFICE, *supra* note 359, at 20; Ellen Nakashima & David Brown, *U.S. Rule on AIDS Drugs Criticized: Ban on Using Aid To Buy Foreign Generics Hinders Treatment, Experts Say*, WASH. POST, July 14, 2004, at A12 (quoting Rachel Cohen of MSF).

371. U.S. GEN. ACCOUNTING OFFICE, *supra* note 359, at 44.

372. *See supra* Subsection II.A.3.ii.

373. For a description of the effort to create FDCs for malaria in Africa and Latin

prequalified a FACT.[374]

B. Pharmaceutical Arbitrage from Canada

Pharmaceutical arbitrage is not just an issue in low and middle income countries; millions of U.S. residents are importing cheaper patented drugs from Canada and elsewhere—the so-called "Boston Tea Party of the 21st Century."[375] Drug imports from Canada should be a textbook example of pharmaceutical arbitrage at work, as PhRMA companies scramble to protect high-priced U.S. markets.

For the larger essential medicines debate, the most salient conclusion from the following analysis is that pharmaceutical arbitrage will flourish, even at relatively low arbitrage ratios below 2:1. Aggressive moves by PhRMA companies and the FDA have not succeeded in stopping the arbitrage. The key factor is the legal ambiguity and moral support for the practice of importing from Canada. Institutions and human behavior matter a great deal when neo-classical economic theory is applied in the real world. In the narrower context of U.S. drug prices, arbitrage from Canada seems unlikely to harm innovation, absent transparent access to PhRMA company data to prove the contrary.

1. The Opportunity for Arbitrage

Patented drug prices in the United States are generally the highest in the world.[376] Most other OECD countries have regulatory structures that

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America, see Press Release, DNDi, Malaria Patients Enter DNDi Clinical Trials (July 2, 2004), http://www.dndi.org/cms/public_html/insidearticleListing.asp?CategoryId=166&SubCategoryId=167&ArticleId=301&TemplateId=1; and DNDi, Fact Sheet, *at* http://www.dndi.org/cms/public_html/insidearticleListing.asp?categoryid=164&articleid=304&templateid=2 (last visited July 18, 2004).

374. WORLD HEALTH ORG., ACCESS TO ARTEMISININ-BASED COMBINATION ANTIMALARIAL DRUGS OF ACCEPTABLE QUALITY (2d ed. 2004), http://mednet3.who.int/prequal/. The Artemether/Lumefantrine FDC is manufactured by Novartis.

375. Senator Joe Lieberman, Democratic Presidential Debate in Goffstown, New Hampshire (Jan. 22, 2004), 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.

376. United States patented prescription drug prices are the highest of any major market, with the possible exception of Japan. Danzon & Furukawa, *supra* note 173, exhibit 3. Generic drugs, unprotected by patents or exclusive marketing periods, are generally priced competitively in the United States. Comparisons of international drug prices should not conflate these categories. Danzon and Furukawa fault other studies for excluding

significantly limit prices for patented pharmaceuticals.[377] Canadian price controls, including the Patented Medicine Prices Review Board[378] help to keep Canadian prices significantly lower than U.S. prices for patented drugs.[379] This significant differential pricing invites consumer arbitrage.

The first phase of the Canadian-U.S. 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

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generics since they represent significant volumes in the OECD. *Id.* at 4. However, generics must be excluded when calculating rents or the potential for arbitrage in patented drugs. Canadian prices are sixty-four percent of U.S. prices for patented drugs, and somewhat higher for generics, yielding a net differential of six percent. *Id.* exhibit 4; *see also* Letter from William K. Hubbard, Associate Commissioner for Policy & Planning, FDA, to Ram Kamath & Scott McKibbin, Special Advocates for Prescription Drugs, State of Illinois (Nov. 6, 2003) (on file with author) [hereinafter Hubbard Letter] (noting that generics are generally cheaper in the United States compared to Canada). Thus the potential for arbitrage lies in the thirty-six percent differential in patented medications, not the six percent overall figure.

377. *See* ROTHNIE, *supra* note 66, at 491 (providing a general, but dated, discussion of EU pharmaceutical price controls); *see also* DANZON ET AL., *supra* note 186 (noting that pharmaceutical companies delay the launch of new drugs in EU countries with strict price controls to reduce the risk of parallel trade).

378. Since 1988, Canada has regulated patented drug prices through the Patented Medicine Prices Review Board, a quasi-judicial board with can bring proceedings against PhRMA companies that charge excessively high prices. MARIA BARRADOS ET AL., 1998 REPORT OF THE AUDITOR GENERAL OF CANADA ¶ 17.93 (1999), http://www.oag-bvg.gc.ca; Robert G. Elgie, Canada's Patented Medicine Prices Review Board: New Approaches, Address to Drug Industry Association Washington Conference on Pharmaceutical Pricing and Reimbursement: What New Variables are at Work? 3-4 (Apr. 16, 1999), http://pmprb.com/cmfiles/sp-dia-e14NRL-482003-7465.pdf. The Board has constrained some patented drug prices in Canada. BARRADOS ET AL., *supra*, ¶17.25. Since the creation of the Board, patented pharmaceutical prices in Canada have increased only one percent 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 ET AL., *supra*, ¶17.50 -17.56; Elgie, *supra*, at 6.

379. Many surveys have documented the price differential between U.S. and Canadian patented pharmaceuticals. *See, e.g.*, RAM KAMATH & SCOTT MCKIBBIN, ILL. OFFICE OF SPECIAL ADVOCATE FOR PRESCRIPTION DRUGS, REPORT ON FEASIBILITY OF EMPLOYEES AND RETIREES SAFELY AND EFFECTIVELY PURCHASING PRESCRIPTION DRUGS FROM CANADIAN PHARMACIES 79 (2003) (thirty-nine percent savings on the drugs that Illinois purchases that could be safely imported from Canada); Danzon & Furukawa, *supra* note 173, exhibit 4 (noting that patented drugs are thirty-six percent cheaper in Canada compared with the United States); *Savings Immense on Canadian Drugs*, WASH. TIMES, Nov. 5, 2003, at A15 (thirty-three percent to eighty percent cheaper for the ten most popular drugs).

sick while in Canada, or who unexpectedly exhausted their U.S. 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 U.S. 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 United States and Canadian drug prices.

These early forms of arbitrage were limited in several ways. Only drugs for outpatient non-emergency use could easily be 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 United States during this phase of the market. Knowledge of the arbitrage opportunity was largely gained by word of mouth or opportune discovery.

i. 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.[380] 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 the last several years, the potential number of buyers expanded again, as U.S.-based companies began to facilitate Internet ordering of pharmaceuticals for unwired consumers, particularly the

380. For a patient with annual out of pocket prescription costs of $2000, a reasonable amount of search costs can be justified to save thirty percent.

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[381] and governments[382] 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,[383] with potential savings of $90.7 million per year.[384] Several other states are exploring similar programs.[385] These state efforts are being blocked by the FDA.

The current level of arbitrage is already significant in the Canadian market. In 2004, the U.S. retail prescription drug market is an estimated $207.9 billion.[386] In October 2003, an FDA official estimated that three million U.S. prescriptions per year were being filled from Canada,[387]

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381. United States-based PBMs are paying claims today from Canadian pharmacies, supporting the patient's decision to import, KAMATH & MCKIBBIN, *supra* note 379, 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.

382. 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 379, at 3, 30.

383. *Id.* at 79-81.

384. *Id.* at 19. This figure is based on the assumption that all employees and retirees will participate.

385. *See, e.g.*, Fred Frommer, *Pawlenty Tries To Win FDA over on Drug Plan*, MINNEAPOLIS STAR TRIB., Jan. 16, 2004 (describing the Minnesota Governor's attempt to win FDA approval for a drug importation plan); Tony Leys, *Vilsack Offers Plan on Canadian Drugs*, DES MOINES REG., Jan. 22, 2004 (describing Iowa's plan); Katherine M. Skiba, *Doyle Makes Case for Buying Cheaper Drugs from Canada*, MILWAUKEE JOURNAL SENTINEL, Feb. 24, 2004, at 1A.

386. Heffler et al., *supra* note 80, exhibit 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. SAGER & SOCOLAR, *supra* note 11, at 4 & n.25.

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

yielding an estimated arbitrage market size of $600 to $700 million in 2003.[388] The IMS Health consulting agency estimates US$1.1 billion (in U.S. prices) in 2003, an increase of seventy percent over 2002.[389] 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,[390] 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;[391] normal U.S. prices will not fall unless the PhRMA companies agree to reduce their monopoly price. If the supply of patented drugs in Canada remains sufficient, a permanent arbitrage opportunity results and will persist for as long as the patent remains in force.[392] With negligible transaction and information costs, a fungible

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388. While the average size of U.S.–Canadian prescriptions is unknown, data from the State of Illinois describe consumer co-pays of at least $40 per prescription, KAMATH & MCKIBBIN, *supra* note 379, at 5, implying a retail price of $200 at a twenty percent co-pay. Recent Canadian estimates suggest a market of $700 to $800 million per year. Tamsin Carlisle, *Canada Cools to U.S. Drug Flow: 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,* PHILA. INQUIRER, Nov. 16, 2003, at A24. Other recent studies have reached similar estimates for the size of the Canadian arbitrage market. SAGER & SOCOLAR, *supra* note 11, at 4 ($695 million in 2003, based on IMS data). The largest U.S. retail drug store chain, CVS, estimates that U.S. patients spend $3 billion a year outside the United States. *US HHS Import Task Force Urged To Curb Overseas Pharma Price Controls,* PHARMA MARKETLETTER, May 17, 2004. By comparison, the domestic U.S. prescription mail order market was $20.7 billion in 2001. NIHCM, *supra* note 63, at 9.

389. Morais, *supra* note 324 (quoting Paul Saatsoglou, IMS Health).

390. CAN. INST. FOR HEALTH INFO., *supra* note 79, at 66. Precise comparisons with U.S. 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 U.S. statistics).

391. PhRMA 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, at W1. These price increases were targeted against drugs in the U.S. arbitrage market. PhRMA 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.

392. A permanent arbitrage opportunity is also present in the EU parallel market, given national price controls and various legal restrictions which keep parallel trade to a manageable size. KANAVOS ET AL., *supra* note 54, at 136 (disproving the price convergence

product in abundant supply, and non-responsive pricing, one would expect a large portion of the available U.S. market to source from Canada, limited only by the capacity of the Canadian market to handle the volume.[393]

Theoretically, Canadian arbitrage may destroy the differential pricing system which kept U.S. drug prices the highest in the world. Erosion of differential pricing might shift consumer surplus from producers to consumers. American consumers might save many billions of dollars on pharmaceuticals, greatly improving financial access. The other side of the coin is that PhRMA companies may lose the lion's share of their worldwide profits.[394] One unasked question is whether this process will result in sub-optimal pharmaceutical rents. Supporters of pharmaceutical companies simply assume that drug innovation will be hindered. So long as total pharmaceutical rents remains supra-optimal, Canadian arbitrage improves consumer welfare without harming innovation.

ii. 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.[395]

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hypothesis).

393. A recent CBO issue brief suggests that the net effect on U.S. prices from Canadian arbitrage will be small. CONG. BUDGET OFFICE, WOULD PRESCRIPTION DRUG IMPORTATION REDUCE U.S. DRUG SPENDING? 15 (2004). The CBO assumed that arbitrage supplies would be successfully interdicted by PhRMA companies, capping the arbitrage at ten to fifteen percent of the U.S. market and assumed no competitive price reductions in the United States. *Id.* at 4-6. Even under the CBO's pessimistic assumptions, the ten year savings to U.S. consumers will be $40 billion. *Id.* at 8. Put another way, PhRMA's displaced sales from legalizing OECD arbitrage will be $40 billion over ten years.

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

395. The classic work is Charles Tiebout, *A Pure Theory of Local Expenditures*, 64 J. POL. ECON. 416 (1956).

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 their products.[396] Other nations, such as Canada, have imposed more restrictive regulatory measures to reduce prices.[397] One perspective on this cross-border arbitrage is that some Americans have imported Canada's pricing regulatory system into the United States for outpatient non-emergency pharmaceuticals.[398] Regulatory arbitrage is at work between the United States 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.[399] The certification proved to be the Achille's heel, since HHS has refused to issue the certification.[400] 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.[401] The Pharmaceutical Market Access Act of 2003, also passed by the House, permitted imports from twenty-five countries with effective NDRAs.[402] The

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396. The industry strongly oppose price controls. *See, e.g.*, Sidney Taurel, *Hands Off My Industry*, WALL ST. J., Nov. 3, 2003, at A14. Taurel is President, Chairman, and CEO of Eli Lilly.

397. Many discussions of Canada's patented pharmaceutical pricing system wrongly assume that it includes mandatory price controls. Canada's Patented Medication Prices Review Board uses 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 ten percent of revenues and grants special pricing consideration to breakthrough drugs. BARRADOS ET AL., *supra* note 378, ¶ 17.56; Elgie, *supra* note 378, at 3-4. Thus, Canada's system is one attempt to optimize the appropriation of rents, striking a balance between cost, quality and access, based upon imperfect data.

398. The American Enterprise Institute identifies this as a major weakness of proposals to permit reimportation from Canada. JOHN E. CALFEE, THE HIGH PRICE OF CHEAP DRUGS (2003), http://www.aei.org/docLib/20030715_%2315530Calfeegraphics.pdf.

399. Medicine Equity and Drug Safety Act of 2000, Pub. L. 106-387, 114 Stat. 1549A-35 (codified at 21 U.S.C. § 384).

400. Sarah Lueck, *Senate Supports Wider Importing of Canada Drugs*, WALL ST. J., June 23, 2003, at A10.

401. 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 reimportation from the EU as well. Save Our Seniors Act of 2003, H.R. 2769, 108th Cong. § 2 (2003).

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

Senate version of the bill reinstated the certification requirement, effectively gutting Canadian importation under the Bush Administration.[403] Most observers would not expect a majority of the U.S. 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.[404]

Another example of regulatory arbitrage involves the efforts of U.S. psychologists to obtain prescribing authority, currently denied to them under U.S. law. Some U.S. psychologists direct their patients to Canadian pharmacies, which accept prescriptions written by U.S. psychologists.[405] This practice will provide empirical evidence of the medical efficacy of prescriptions by U.S. 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 competitive analysis of regulatory structures and allows market participants to influence the debates with diminished intermediation by interest groups.[406]

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403. Medicare Prescription Drug Improvement and Modernization Act of 2003, 21 U.S.C. § 804 (2000); *see also* Sarah Lueck, *Senate Supports Wider Importing of Canada Drugs*, WALL ST. J., June 23, 2003, at A10. A subsequent administration could certify safety and cost-effectiveness and begin importation from Canada without additional Congressional legislation.

404. Henry J. Aaron, *Should Public Policy Seek To Control the Growth of Health Care Expenditures?*, W3 HEALTH AFF. 28-31 (2003) ("The chances that we will adopt the Canadian or French health care systems 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 398.

405. Linda Temple, *Who Gets To Prescribe? Psychologists Send Drug Orders to Canada, Spark a Medical Debate*, USA TODAY, Dec. 18, 2003, at D10.

406. Alvarez and Trachtman note that regulatory arbitrage may or may not have positive effects, depending upon the condition of spillovers (negative externalities). 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 destabilize the system, and force OECD countries to re-allocate jurisdiction on drug price regulation. Efficient re-allocation of jurisdiction is the primary theme in 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

iii. 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 United States employs a virtual arbitrage system in requiring certain discounts for drugs purchased under Medicaid, discounts which reference other "best" prices.[407] West Virginia recently established a state agency which adopted the Federal Supply Schedule as a soft reference price for drug purchases by the state.[408] If West Virginia succeeds in lowering drug prices, many other states will likely 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.[409] 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 markets into high income markets must be blocked if differential pricing is to be supported for essential medicines.[410]

Without clear data on the optimality of pharmaceutical rents, 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 and the arbitrageur; however it begs the question to assume that arbitrage will reduce pharmaceutical rents to a sub-optimal level. One should not assume that the externality is negative. It is possible that West Virginia's use of an external reference price retains supra-optimal innovation incentives while dramatically lowering the state's costs and improving access.

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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 Chi. John M. Olin Law & Econ., Working Paper No. 188, 2d Series, 2003).

407. 42 U.S.C. § 1396r-8 (2000) (using reference prices to calculate drug prices and drug rebates under Medicaid).

408. WEST VIRGINIA REPORT, *supra* note 175, at 1-7.

409. 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 ECON. L. 637 (1998). These claims are hotly disputed by proponents of parallel trade in pharmaceuticals. *See, e.g.*, WEST & MAHON, *supra* note 327.

410. *See supra* Subsection II.B.2.

2. Responses to Canadian-U.S. Arbitrage

The current efforts to hinder Canadian arbitrage include legal interdiction, increasing transaction and information costs, and selectively controlling drug supplies shipped to Canada.

i. 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 the legality of the transaction, eligibility for reimbursement from third parties, and the counterparty risk of fraud.[411]

In the first two phases of Canadian arbitrage,[412] the transactions were clearly legal under U.S. 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.[413]

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,[414] 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.

411. 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.

412. *See supra* Subsection II.B.1.

413. FDA, Personal Use Import Policy, http://www.fda.gov/ora/import/pipinfo.htm (Apr. 3, 1998).

414. *See, e.g.*, United States v. Ramsey, 431 U.S. 606 (1977) (holding that customs officials are permitted to intercept mail for contraband).

Beginning in 2003, the enforcement environment changed.[415] Federal and state officials are currently attacking Internet pharmaceutical arbitrage on multiple fronts. The FDA is aggressively enforcing against U.S. companies involved in the trade.[416] The Customs Department has posted clarifications of the personal use exception to discourage importation.[417] 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.[418] The FDA has sued regional facilitators such as Rx Depot for assisting in the importation of prescription drugs.[419] The FDA and state pharmacy investigators have also purchased prescription drugs in undercover operations.[420] Direct interdiction would include enforcement actions against consumers, but arresting grandparents for purchasing Canadian Lipitor is not politically viable.

Canadian arbitrage was born in conditions of legal uncertainty, and continues with a zone of legal protection around the consumers. In addition, the consumers occupy the moral high ground of gaining access to an important drug at market rates. These conditions allowed arbitrage to take root and grow. Citizens and governments which would never consider importing cocaine are buying Canadian drugs over the Internet.

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

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415. Thomas M. Burton, *The FDA Begins Cracking Down on Cheaper Drugs from Canada*, WALL ST. J., Mar. 12, 2003, at A1.

416. 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); Gardiner Harris and Monica Davey, *U.S. Steps Up Effort Against Drug Imports*, N.Y. TIMES, Jan. 24, 2004, at C1; *Recent FDA/U.S. Customs Import Blitz Exams Continue To Reveal Potentially Dangerous Illegally Imported Drug Shipments*, FDA NEWS, Jan. 27, 2004.

417. U.S. Customs & Border Protection, Medication/Drugs, http://www.cbp.gov/xp/cgov/travel/alerts/medication_drugs.xml (last visited Feb. 15, 2004).

418. 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. Becker v. W. Va. Board of Pharm., No. 03-C-1237, slip op. at 11-12 (W. Va. Cir. Ct. Nov. 3, 2003).

419. 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., 290 F. Supp. 2d 1238 (N.D. Okla. 2003).

420. Rx Depot Transcript, *supra* note 387, at 16-40.

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.[421] 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.[422] These consumers are relying on the effectiveness of Health Canada's Therapeutic Product Directorate (TPD), assuming that Canadian drugs are generally as safe as U.S. drugs regulated by the FDA. If the safety or equivalence of drugs from Canadian Internet pharmacies is in doubt, this assumption dissolves and risk-averse consumers are less likely to arbitrage. Supporters of importation take the opposite tack. 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 more secure than that of the United States.[423]

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.[424] Questions have been raised as to whether the drugs are produced and transported under FDA standards of safety.[425] Labeling issues, such as the Canadian label for Accutane, have been identified.[426] 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.[427]

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421. PHILIPS, *supra* note 43, at 187-200.

422. Raising search costs for these consumers should hinder arbitrage and support differential pricing. *See* PHILIPS, *supra* note 43, at 187-200.

423. KAMATH & MCKIBBIN, *supra* note 379, at 11-16 (finding Canadian and U.S. 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).

424. *See, e.g., Recent FDA/U.S. Customs Import Blitz Exams Continue To Reveal Potentially Dangerous Illegally Imported Drug Shipments*, FDA NEWS, Jan. 27, 2004.

425. Rx Depot Transcript, *supra* note 387, at 16-158.

426. *Id.* at 77 l. 22 (cross-examination of Melvin Frank Szymanski, consumer safety officer, FDA).

427. *Savings Immense on Canadian Drugs*, WASH. TIMES, 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

At one level, these accusations prove too much. Counterfeit and unsafe drugs are found in the U.S. market generally and are not confined to the Internet supply chain.[428] The FDA does not want to undermine consumer confidence in the U.S. drug supply, but to distinguish the U.S. domestic supply from international Internet sources. Thus, the FDA opposes all international pharmaceutical arbitrage into the United States.

c. The Special Case of Reimportation

Questions about production safety, equivalence, and labeling are reduced for a segment of this market known as reimportation. 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 U.S. government has long encouraged pharmaceutical research and production through generous tax incentives under Section 936 of the Internal Revenue Code.[429] Many drugs produced in these U.S. plants are both sold into the U.S. market as well as exported to nations like Canada. When these drugs make the return trip back to the United States, the process is called reimportation.

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 safe, efficacious, and properly labeled for Canadian use. The FDA worries about errors in shipping and handling from Canada to the consumer,[430] 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 reimportation solely on that basis.[431] But the FDA has not shown that the Canadian drug supply is less safe. Rx Depot was one of the largest facilitators of importing prescription drugs from Canada. The FDA sued Rx Depot, demanding that importation cease. At the Rx Depot trial in October 2003, the FDA was unable to say that Canadian drugs were unsafe or had injured Americans.[432]

India and China and all those countries we have health concerns about.") (quoting Sen. John B. Breaux, D-La); Hubbard Letter, *supra* note 376 (noting one instance of a Canadian website shipping an Indian drug).

428. *'Lipitor' Surfaces in Counterfeit Probe*, WALL ST. J., Dec. 8, 2003, at B8; Daniel Yee, *CDC: Seniors Prescribed Dangerous Drugs*, LAS VEGAS SUN, Feb. 9, 2004.

429. Puerto Rico and Possessions Tax Credit, 26 U.S.C. § 936 (2000).

430. Rx Depot Transcript, *supra* note 387, at 29-31.

431. *Id.* at 28, 76-77.

432. *Id.* at 138-41. *But see* Hubbard Letter, *supra* note 376 (claiming that Internet sales

The most thorough recent analysis of this question concludes that the Canadian drug supply is actually safer on balance than that of the United States. 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.[433] The EU has many years of experience with parallel trade in pharmaceuticals, without significant safety issues.[434]

ii. Reducing Arbitrage Supply

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. In European markets, PhRMA companies successfully restrict supply to curb parallel trade.[435] Conversely, theory suggests that 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 that sell to the United States market. These pharmacies have been threatened with a refusal to deal unless the cross-border sales cease.[436] 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 and legality of attempts to restrict supply to Canada.[437]

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from Canada will be more open to counterfeiting).

433. KAMATH & MCKIBBIN, *supra* note 379, at 1-5.

434. WEST & MAHON, *supra* note 327.

435. Janice Haigh, *Parallel Trade: What Next?*, 9 PHARMA PRICING & REIMBURSEMENT 295, 297-98 (2004).

436. Tamsin Carlisle, *Pfizer Pressures Canadian Sellers of Drugs to U.S.*, WALL ST. J., Jan. 14, 2004, at A6; Tamsin Carlisle, *Some Online Pharmacies Aren't Filling Big Orders Due to Fears of Shortages*, WALL ST. J., Dec. 26, 2003, at A9; John O'Connor, *Canadians Warn of Rx Shortage*, CHI. SUN-TIMES, Nov. 13, 2003, at 18; Tony Pugh, *Low-Cost Drug Sales to U.S. Should Stop, Canadian Group Says*, PHILA. INQUIRER, Nov. 16, 2003, at 18. Similar restrictions have been employed for many years to hinder parallel trade in Europe, Maskus & Ganslandt, *supra* note 55, at 69-70, with limited effectiveness, WEST & MAHON, *supra* note 327. For the effects of the same tactic on a national level, see DANZON ET AL., *supra* note 186.

437. KAMATH & MCKIBBIN, *supra* note 379, at 22 ("[W]e 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,

Members of Congress have asked the United States Attorney General to investigate whether antitrust laws are being violated,[438] and traditional Canadian pharmacies are complaining about the impact of drug company restrictions on their domestic operations.[439]

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 United States 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.[440] If the concern is truly for patient safety, supply restrictions are a crude and counterproductive tool.

b. Reducing Demand in the United States with a Medicare Prescription Drug Benefit

Pharmaceutical companies also restrict demand in the United States. The current market is mostly non-emergency outpatient drugs. For the Medicare population, these drugs have historically not been covered. In 2003, the U.S. Congress for the first time passed a Medicare prescription drug act, as PhRMA reversed its historic opposition and embraced a market-based third party reimbursement plan in Medicare for outpatient drugs.[441] The new Medicare drug benefit will reduce consumer demand for

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limiting supply to Canadian pharmacies may risk their Canadian patent protection; second, as the Minnesota Attorney General and Illinois Attorney General are currently investigating any concerted effort by the pharmaceutical companies to limit supply may violate U.S. antitrust laws.").

438. Gardiner Harris, *Some in Congress Seek Inquiry over Drug Supply to Canada,* N.Y. TIMES, Nov. 1, 2003, at C2.

439. Carlisle, *supra* note 436; O'Connor, *supra* note 436; Pugh, *supra* note 436.

440. KAMATH & MCKIBBIN, *supra* note 379, at 11-18 (explaining that Canada's drug distribution system does not rely on intermediates to the same extent as the U.S. system and that increasing reliance on intermediates increases the risk of counterfeit drugs).

441. Prescription Drug and Medicare Improvement Act of 2003, 42 U.S.C.A § 1395, 1395-1430 (West 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

arbitrage in an important population and thus support differential pricing.

3. Implications of Optimality for Canadian-U.S. Arbitrage

Mindlessly blocking pharmaceutical arbitrage between high income countries 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.

The United States should permit functional pharmaceutical arbitrage, particularly with countries with NDRAs similar to the FDA. Regulatory resources would be devoted to coordination with these governments to ensure the integrity of the supply chain. PhRMA companies bemoan this approach as destructive of long-term research incentives. This is an overly simplistic assessment, for it assumes that pharmaceutical rents would be sub-optimal at undifferentiated high income market prices. If, in fact, Canadian prices are supra-optimal, then Canada is not free riding on American R&D.[442] Optimal pharmaceutical rents would be achieved at prices between current U.S. and Canadian prices. PhRMA companies would be able to compensate for reduced unit prices by increasing volume.

If Canadian prices currently result in supra-optimal pharmaceutical rents, then extending Canadian prices to the United States will do no harm to innovation. This astonishing possibility would greatly reduce U.S. 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.[443] If optimality lies somewhere between U.S. and Canadian prices, then U.S. prices could be decreased by some amount without harming innovation. Modest levels of arbitrage and additional price transparency may achieve this result.

Finally, the Canadian experience suggests that PhRMA 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 expenditures per capita have been rising

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follow the same trend line.

442. *See* Kevin Outterson, *Free Trade Against Free Riders*, 9 PHARMA PRICING & REIMBURSEMENT 254-55 (2004).

443. BARRADOS ET AL., *supra* note 378, ¶ 17.11 (noting that Canadian drug companies agreed to increase R&D to ten percent of sales by the end of 1996). For current data on Canadian pharmaceutical R&D, see Rx&D, *at* http://www.canadapharma.org (the official trade association website).

by 10.2% annually. [444] Companies increase their profits in declining unit price markets by increasing unit sales[445] and by developing new drugs.[446] If profits are stable or increasing, innovation is not harmed. 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 high income market internal differential pricing system would put the ball in PhRMA companies' court to demonstrate whether the resulting pharmaceutical 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 and secret company data.

CONCLUSION

The head of the U.S. global AIDS effort, Ambassador Randall Tobias, is 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."[447] I beg to differ. Not only are ARVs still not widely available at marginal cost in developing countries, but drug pricing remains unaffordable for other global diseases such as cancer and heart disease in low and middle income markets. The industry prefers to turn off the media spotlight and assume that access problems were adequately addressed at Doha and Cancun, or will be dealt with by PEPFAR. Meanwhile, global public health catastrophes continue to mount. For some of these conditions, we possess effective therapies that can be provided on nonrival terms but are withheld from the poor because of fears of inadequate pharmaceutical rents.

Health care public policy should not be chained to innovation; it must also champion access, whether in Africa or Akron. The theory and praxis of pharmaceutical arbitrage suggests that pharmaceutical access may be greatly improved, at a modest cost, without damaging optimal innovation.

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444. CAN. INST. FOR HEALTH INFO., *supra* note 79, fig.18 (reporting, based on 2002 data, the stable to declining Patented Medicine Price Index since the introduction of the Patented Medicine Prices Review Board).

445. *Id.* fig.14 (reporting annual growth rate of per capita prescribed drug expenditures of 10.2% from 1997-2000).

446. *Id.* at 33-43.

447. Robin Wright, *A CEO To Direct the AIDS Battle: Former Eli Lilly Chief Comes out of Retirement*, WASH. POST, Feb. 13, 2004, at A25.