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

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Kevin Outterson*

I. 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 for 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 discussions, two sets of arguments are usually forwarded. Some argue that pharmaceutical prices are necessarily high because

* Associate Professor of Law, West Virginia University College of Law. Special thanks to the American Society of Law, Medicine & Ethics September 2003 Health Law Young Scholars Workshop and the West Virginia University College of Law Faculty Workshop for helpful comments and suggestions. This research was supported by a Hodges Research Grant from the West Virginia College of Law. An early draft of this Article was prepared during my tenure as a Visiting Fellow at the Lauterpacht Research Centre for International Law at the University of Cambridge. Helpful comments were received from many people, including Frances Miller, Ben Moulton, Charity Scott, Ana Iltis, Timothy D. McBride, Thomas Greaney, Jesse Goldner, Sidney Watson, Sandra Johnson, Nicolas Terry and Aidan Hollis, as well as from participants at the New Economic Windows 2004 conference in Salerno.

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

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 break-through therapies.⁴ Others counter that much of the profits going to pharmaceutical companies⁵ are used for marketing and other expenses rather than 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—

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, 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 (Nov. 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 which 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 <http://www.phrma.org>. The international trade association of PhRMA company groups is the International Federation of Pharmaceutical Manufacturers Associations (IFPMA), see <http://www.ifpma.org>. Generic drug companies have their own trade associations, such as GPhA, www.gphaonline.com. 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.

⁶ See, e.g., Marcia Angell, *The Truth About Drug Companies*, 51 N.Y. Rev. of Books (July 15, 2004).

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) available at: <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), available at <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 *supra* *ECONOMICS OF ESSENTIAL MEDICINES*, *supra* note 3, at 209-231.

do not always reflect 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, which provide financial support for global R&D innovation¹¹ and thus to buttress voluntary differential pricing schemes (e.g., the AIDS initiative) that benefit low income countries.¹² So long as R&D costs continue to be partially reimbursed through the price mechanism,¹³ the conventional wisdom holds that pharmaceutical arbitrage is a major threat to 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 pharmaceutical arbitrage is being used to justify expanding pharmaceutical IP rights and related powers of appropriation. 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 One of the Article establishes a theoretical framework for understanding pharmaceutical markets and innovation, using the heuristic device of *optimal patent rents* to explore pharmaceutical arbitrage. 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 Two 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 optimal patent rent heuristic indicates that several forms of pharmaceutical arbitrage are beneficial, delivering lower prices to consumers without harming innovation. Arbitrage

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

¹¹ Tom Blackwell, *Canada's Drug Pricing Unfair, U.S. Alleges: Pharma Companies Back Plan to Restrict Cross-Border Sales*, Nat'l Post, May 3, 2004, at A6; Gardiner Harris, *Cheap Drugs from Canada: Another Political Hot Potato*, N.Y. Times, Oct. 23, 2003; *but see* ALAN SAGER & DEBORAH SOCOLAR, DO DRUG MAKERS LOSE MONEY ON CANADIAN IMPORTS? (Boston Univ. Sch. of Pub. Health, Data Brief No. 6, April 15, 2004) available at <http://www.healthreformprogram.org>.

¹² PATRICIA M. DANZON & ADRIAN TOWSE, DIFFERENTIAL PRICING FOR PHARMACEUTICALS: RECONCILING ACCESS, R&D AND PATENTS 28-29 (AEI-Brookings Joint Center for Regulatory Studies, Working Paper No. 03-7, July 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) available 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) available at http://www.earthinstitute.columbia.edu/cgsd/accesstomedicines_papers.html.

within and between high income markets, such as the Canadian Internet sales to the United States, will not harm innovation if patent 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.¹⁴ Therefore, in markets which are unlikely to contribute importantly to optimal global patent rents, the shackles of intellectual property law and other forms of appropriation are both unnecessary and dangerous; such laws should completely step 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. Low transaction cost compulsory licenses are suggested, consistent with the needs for innovation.

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 patent rents, access can be expanded to all categories of global diseases, including cancer and heart disease, without damaging innovation.

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.

PART ONE: THE THEORY OF PHARMACEUTICAL ARBITRAGE

II. 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.¹⁵ 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

¹⁴ This term is defined in Section II *infra*.

¹⁵ 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.

consent, due process or some important public policy.¹⁶ In the language of economics, goods and services are “appropriable.”

In common law, knowledge was not considered personal property,¹⁷ perhaps because the use of information is subject to at least two peculiar characteristics. First, knowledge is generally inappropriable or nonexcludible: It is generally more difficult to exclude other persons from using it. (This Article uses the terms interchangeably.) Second, knowledge is nonrival: While physical goods like corn or wheat are exhausted when used, knowledge may be used without exhaustion.¹⁸

The nonrival nature of knowledge permits its widest possible dissemination without creating shortages, a potential boon for humanity.¹⁹ The nonrival nature of knowledge is a wonderful thing. 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 it without compensating the innovator. The innovator cannot capture the positive externality (or consumer surplus), undermining one incentive to innovate.

The economic model is overly pessimistic. Inventive knowledge expanded in the centuries prior to the adoption of patent law. Important books were written before the

¹⁶ 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.*, STEWART E. STERK, WHAT’S IN A NAME? THE TROUBLESOME ANALOGIES BETWEEN REAL AND INTELLECTUAL PROPERTY 1-3 (Benjamin N. Cardozo School of Law, Jacob Burns Institute for Advanced Legal Studies, Working Paper No. 88, 2004); MARK A. LEMLEY, PROPERTY, INTELLECTUAL PROPERTY, AND FREE RIDING 3-17 (John M. Olin Program in Law and Economics, Working Paper No. 291, Aug. 2004).


¹⁷ *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, *The Rise of Intellectual Property, 700 B.C. – A.D. 2000: An Idea In The Balance*, DAEDALUS 26-45 (Spring 2002) (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.

¹⁸ 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. [AU: **Please provide citation to theoretical work on non-diminishing value of knowledge.**] [ED: **I am not aware of such literature. I have raised this point with Mark Lemley at Stanford as well. I think we can just leave it unreferenced**]

¹⁹ This point is occasionally overlooked. In his critique of the consequences of TRIPS for pharmaceutical access, 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). 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.

Statute of Anne.²⁰ This can at least be partially explained by non-economic motives for research, such as curiosity or personal achievement.²¹ In most industries, patents play a relatively minor role in promoting innovation.²²

Nevertheless, pharmaceutical research companies strongly embrace this neo-classical innovation model.²³ They argue that without IP laws first 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 tion²⁴ to this impasse—“promot[ing] the progress of science and useful arts, by securing for limited times, to authors and

²⁰ Today’s industrialized countries are relatively recent converts to the cause of strong IP laws. DRAHOS, *supra* note 2, at 29-38.

²¹ The open source movement in science is built upon such factors, as articulated by several leading scientists. Stephen M. Maurer, Arti Rai & Andrej Sali, *Finding Cures For Tropical Diseases: Is Open Source an Answer?* in BIOTECHNOLOGY: ESSAYS FROM ITS HEARTLAND 33-37 (Lynn Yarris ed., 2004) available at www.saililab.org/publications; Sir John Sulston, *Open and Collaborative Movements in Science*, (oral presentation at the Trans Atlantic Consumer Dialogue Future of WIPO Workshop, Geneva, Sept. 13, 2004); 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.

²² 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, Jan. 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, Feb. 2000) (forty years of empirical data demonstrates that patents don’t improve innovation, with exceptions in pharmaceuticals; study concludes that patents are not the most significant mechanisms for appropriating returns to innovation in most industries, with secrecy, lead time and complimentary capabilities leading); 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 AMER. 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.

²³ One prominent source on R&D expenditures by PhRMA companies is Joseph A. DiMasi, Ronald W. Hansen & Henry G. Grabowski, *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. of Health Econ. 151 (2003). These claims are defended vigorously by PhRMA and its members. *See, e.g.*, 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); ERNST & YOUNG LLP, PHARMACEUTICAL INDUSTRY R&D COSTS: KEY FINDINGS ABOUT THE PUBLIC CITIZEN REPORT (AUG. 8, 2001) available at www.phrma.org.

²⁴ *See, e.g.*, TOMAS J. PHILIPSON & STÉPHANE MECHOULAN, INTELLECTUAL PROPERTY & EXTERNAL CONSUMPTION EFFECTS: GENERALIZATIONS FROM PHARMACEUTICAL MARKETS 3, 8, 14-15 (Nat’l Bureau of Econ. Research, Working Paper No. 9598, April 2003) (“In the private case, it is well-understood that efficient competition ex-post leads to insufficient R&D incentives ex-ante, which is of course the common second-best rationale for patents”) (at 3). For a timely recognition that a bare patent does not equal the clear right to exclude, *see* MARK A. LEMLEY & CARL SHAPIRO, PROBABILISTIC PATENTS (forthcoming in the Journal of Economic Perspectives) July 14, 2004. Lemley & Shapiro’s analysis is not specific to pharmaceuticals, where multiple patents and other appropriation strategies heighten the degree of exclusion, as discussed in Section IV *infra*.

inventors the exclusive right to their respective writings and discoveries.”²⁵ IP laws create the Constitution’s favorite monopolies.²⁶ Currently, under U.S. federal law and the TRIPS Agreement, the patent period is not less than twenty years after filing.²⁷

The social costs of making pharmaceutical knowledge appropriable are generally three-fold. The cumulative effect of these laws allows the 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.²⁸ Second, these higher prices hinder medical access, directly impacting the health of many low income people globally, as demonstrated in Section VI below. Finally and most generally, appropriation by necessity delays the entry of knowledge into the public domain and thus may hinder cumulative innovation.²⁹

The perceived tension between the development and dissemination of knowledge permeates the most compelling issues in pharmaceutical IP policy. Patent doctrines such as scope,³⁰ experimental use,³¹ and fair use³² are also battlegrounds in the struggle

²⁵ U.S. CONST. art. I., § 8, cl. 8.

²⁶ 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.

²⁷ TRIPS, *supra* note 1, at art. 33. TRIPS permitted many developing countries to implement on a delayed basis. TRIPS, *supra* note 1, at 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. World Trade Org., Doha WTO Ministerial 2001, *Declaration on the TRIPS Agreement and Public Health*, WT/MIN(01)/DEC/2, at ¶ 7 (Nov. 20, 2001) [hereinafter *Doha Declaration on TRIPS*]. Despite these concessions, all but three of African 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 (Study Paper 7 for the Commission on Intellectual Property Rights (undated, cir. 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.

²⁸ James Love, Statement of Essential Inventions, Inc. to the Commission on Intellectual Property Rights, Innovation and Public Health 2 (April 5, 2004). [SC: BB as speech/address]

²⁹ See *supra* nn. 119-120 and text accompanying.

³⁰ Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839 (1990) *passim* (examining the potential role of patent breadth in fine tuning the efficiency of the patent system). Many economic studies examine elements of this question. See, e.g., WILLIAM D. NORDHAUS, INVENTION, GROWTH, AND WELFARE: A THEORETICAL TREATMENT OF TECHNOLOGICAL CHANGE 70-90 (1969) [hereinafter NORDHAUS, INVENTION, GROWTH & WELFARE]; F.M. Scherer, *Nordhaus’ Theory of Optimal Patent Life: A Geometric Reinterpretation*, 62 AM. ECON. REV. 422-27 (1972) [hereinafter Scherer, *Optimal Patent Life*]; William D. Nordhaus, *The Optimum Life of a Patent: Reply*, 62 AM. ECON. REV. 428 (1972) [hereinafter Nordhaus, *The Optimum Life of a Patent*]. For a recent example, see PHILIPSON & MECHOULAN, *supra* note 24, at 8-13.

³¹ 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).

between innovation and the public domain.³³ This Article locates additional laws in the policy battleground as well. If too many laws support appropriation (i.e., excessive IP rights and excessive restrictions on nonrival use), the system needlessly raises cost and restricts access to important pharmaceuticals.³⁴ 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 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.

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.³⁵

III. Differential Pricing and Pharmaceutical Arbitrage

A. 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.³⁶

³² Maureen A. O'Rourke, *Toward a Doctrine of Fair Use in Patent Law*, 100 COLUM. L. REV. 1177 (2000).

³³ Dam, *supra* note 26, at 261-68.

³⁴ This point assumes that increased consumption of patented pharmaceuticals creates net positive externalities, i.e. that society would benefit from increased access and consumption of the drug. PHILIPSON & MECHOULAN, *supra* note 24, at 9.

³⁵ http://europa.eu.int/comm/commissioners/lamy/speeches_articles/spla233_en.htm (visited June 15, 2004). [SC: Cite as a speech/address].

³⁶ Price discrimination is the term generally utilized in the economic literature, but should not be confused with price discrimination under the Robinson-Patman Act, 15 U.S.C. §§13-13b, 21a (2004). This Article follows the usage most common in the essential medicines literature: differential pricing. Tiered pricing, 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, Apr. 22, 2002).

Indeed, differential pricing is common: The same product is frequently sold at different net prices to various buyers.³⁷ The seller charges what each market segment will bear.³⁸ 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.³⁹ First-degree price discrimination is also known as perfect price discrimination, since it fully extracts all consumer surplus for the benefit of the producer,⁴⁰ providing cash flow for pharmaceutical innovation but impairing access through higher consumer cost. 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.⁴¹ 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.⁴² 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.⁴³ The primary focus of this Article is third-degree price discrimination, but the more general term, differential pricing, will typically be used. The term 'voluntary differential pricing' in this Article will refer specifically to third-degree price discrimination, as distinguished from second-degree price discrimination such as price controls imposed by monopsonistic payor governments.

³⁷ This particular definition is found in LOUIS PHILIPS, *THE ECONOMICS OF PRICE DISCRIMINATION* 6, 17 (1983).

³⁸ 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, *UNIFORM PHARMACEUTICAL PRICING: AN ECONOMIC ANALYSIS* 5-6, 9-10 (American Enterprise Institute for Public Policy Research, 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 37, at 9.

³⁹ The classic description of first-, second-, and third-degree price discrimination is found in ARTHUR CECIL PIGOU, *THE ECONOMICS OF WELFARE*, CH. 17 [AU: Please provide relevant pages – either entirety of Ch. 17 or subsection thereof][ED:ch 17 is fine] (4th ed. 1920). A helpful summary of Pigouvian price discrimination may be found in PHILIPS, *supra* note 37, at 11-14.

⁴⁰ Perfect from the perspective of the selling firm, rather than the consumer. PHILIPS, *supra* note 37, at 158.

⁴¹ PIGOU, *supra* note 39, at 280.

⁴² *See* PIGOU, *supra* note 39; PHILIPS, *supra* note 37, at 12-13.

⁴³ 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.

Differential pricing is endemic to pharmaceutical markets.⁴⁴ 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 (such as Canada, the United States, and South Africa) and among different buyers or payor classes within countries (examples in the U.S. include Medicare, Medicaid, Veterans Affairs, federal employees, private health plans, and individuals). One form of second-degree differential pricing occurs when price controls are imposed.

B. Pharmaceutical Arbitrage

Pharmaceutical arbitrage is the theoretical nemesis of differential pricing.⁴⁵ While differential pricing assumes that the first purchaser is the 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.⁴⁶ 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,⁴⁷ 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 potentially harms innovation by hindering appropriation by pharmaceutical companies. As will be seen later, the empirical reality of pharmaceutical

⁴⁴ See Sections VI.A and VII.A *infra*. 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; It [SC: sic?][ED: yes] 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.”)

⁴⁵ For a classic account of the interplay between arbitrage and differential pricing, see Philips, *supra* note 37, at 14-16. A recent study in 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: A STAKEHOLDER ANALYSIS 15-16 (Special Research Paper, London School of Economics and Political Science, Jan. 2004) available at <http://www.lse.ac.uk/collections/LSEHealthAndSocialCare/documents/otherpaperseries.htm>.

⁴⁶ 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 THE 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 *infra* Section IV.C.1.

⁴⁷ Philips, *supra* note 37, at 18.

arbitrage departs from the neo-classical model in significant ways.⁴⁸ This Article recognizes that pharmaceutical arbitrage may be either helpful or dysfunctional to consumer welfare.

IV. 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.⁴⁹ Each affects the degree of appropriation in pharmaceutical markets, and thus, the balance between access and innovation.

A. Contract

Private ordering may support differential pricing: The contract between a buyer and seller may expressly or implicitly forbid arbitrage.⁵⁰ If the customer breaches the agreement, the seller can pursue contractual remedies to punish arbitrage. 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 shrinkwrap 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.⁵¹ 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 appropriation.

B. 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, then consumers can cross the price discriminating market segments by choosing the lowest price.⁵² However, producers rarely concede strict fungibility;

⁴⁸ See *infra* Section VI.C.3.

⁴⁹ See Jonathan M. Barnett, *Private Protection of Patentable Goods*, 25 CARDOZO L. REV. 1251 (2004).

⁵⁰ 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 37, at 151-153. A more recent example is the software industry's widespread use of non-transferable licenses. These are most often clickwrap or shrinkwrap 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.

⁵¹ Case C-306/96, *Javico International and Javico AG v. Yves Saint Laurent Parfums SA*, 1998 E.C.R. I-1983, [1998] 5 C.M.L.R. 172 (1998).

⁵² Berndt, *supra* note 38, at 8-10. Philips, *supra* note 37, at ch. 1.

marketing efforts are deployed to influence consumers and reduce their willingness to make substitutions, thus supporting differential pricing.⁵³ This process generally occurs 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 physicians⁵⁴ with their marketing efforts: Overall, U.S. promotional spending on prescription drugs in 2000 totaled \$15.7 billion.⁵⁵ Even after generic entry, these marketing efforts are remarkably effective in retaining market share.⁵⁶ Finally, transaction costs also influence the ease of substitution. If laws raise arbitrage transaction costs, product differentiation is supported and arbitrage is hindered.

C. Government Regulation of Pharmaceutical Appropriation

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).

⁵³ 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 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.

⁵⁴ 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. NIHCM FOUND., PRESCRIPTION DRUGS AND MASS MEDIA ADVERTISING 5 (2000). 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.* at 7; Schneider, *supra* note 4, at 26-36 (fraud cases); Department of Health and Human Services, Compliance Program Guidance for Pharmaceutical Manufacturers, 68 FED. REG. 23731, 23735-38 (May 5, 2003). The industry has also taken steps to suppress negative research. *See* Angell, *supra* note 6, at 12; NAT'L INSTS. OF HEALTH, REPORT OF THE NATIONAL INSTITUTES OF HEALTH BLUE RIBBON PANEL ON CONFLICT OF INTEREST POLICIES 1-5 (May 5, 2004 draft) available at http://www.nih.gov/about/ethics_COI_panelreport.htm [hereinafter NIH, CONFLICT OF INTEREST].

⁵⁵ NIHCM, *supra* note 54, at fig. 3. Approximately one third related to one-on-one meetings with doctors, visits to hospitals, or conferences, and only a portion of that could be considered educational. The largest marketing expense is for free drug samples (\$7.9 billion in 2000). *Id.* at 5. In 2000, U.S. unit sales of the fifty most heavily advertised drugs rose at six times the rate of other drugs. *Id.* at 7 (by number of prescriptions).

⁵⁶ CONGRESSIONAL BUDGET OFFICE, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY xii-xiii (July 1998) [hereinafter CBO, INCREASED COMPETITION].

1. Intellectual Property (IP) Laws

IP laws support pharmaceutical differential pricing by creating legally enforceable rights, which in turn support appropriation. Pharmaceutical patents prevent substitution during the patent period by identical compounds. Trademarks support brand identification and differentiation of products to consumers, hindering consumer confusion or unintended substitution.⁵⁷ The government may also seize counterfeit or improperly diverted drugs.⁵⁸

In many countries, the first sale of a patented product exhausts the public law rights of the patent holder for that item.⁵⁹ This exhaustion rule is a necessary condition⁶⁰ to legal domestic arbitrage, as it permits domestic resale by the purchaser without the permission of the patent holder.⁶¹ Exhaustion may be applied on a domestic or an international basis. The domestic exhaustion rule renders parallel imports illegal while the international exhaustion rule removes patent law barriers to international parallel trade.⁶² U.S. law only recently rejected the international patent exhaustion rule,⁶³ and the

⁵⁷ 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).

⁵⁸ For an interesting story on the diversion of Serostim within the U.S., see Christopher Windham, *Cracking Down on Illicit Use of AIDS Drugs*, WALL ST. J., Jan. 19, 2004, at B1.

⁵⁹ ROTHNIE, *supra* note 57, at 125-42 (Anglo-Commonwealth patent law), 143-150 (U.S. patent law).

⁶⁰ 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 57, at 477, 494-97. *See generally* DG Trade, *supra* note 36, at § 3.

⁶¹ Domestic parallel trade in pharmaceuticals is legal within the EU and the U.S.. *See, e.g.*, Case 187/80, *Merck v. Stephar and Exler*, 1981 E.C.R. 2063, [1981] 3 C.M.L.R. 463 (parallel drug trade is legal in the EU); Donald S. Chisum, *Chisum on Patents* §16.03[2] (2003) (the 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 (unilateral acts by pharmaceutical company to choke off supply of drugs to parallel exporters is not actionable under EU law) and *Glaxo Group Ltd v. Dowelhurst Ltd* [2004] EWCA Civ 129, [2004] All ER (D) 126 (Mar) (requiring repackaging in some cases to protect the trademark).

⁶² DG Trade, *supra* note 36, at §3.1 (“A country providing for international exhaustion effectively makes parallel imports legal, while a country (or regional group) that provides for national (or regional) exhaustion enables rightholders to act against such imports”). TRIPS does not commit to a position on exhaustion, specifically reserving the issue to domestic law. TRIPS, *supra* note 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.*, JEAN O. LANJOUW, INTELLECTUAL PROPERTY AND THE AVAILABILITY OF PHARMACEUTICALS IN POOR COUNTRIES 19-20, n.29 (Ctr. for Global Dev’t, Working Paper No. 5, April 2002), *reprinted in* 3 INNOVATION POLICY AND THE ECONOMY (2002) [hereinafter Lanjouw, Intellectual Property]; and JOHN H. BARTON, DIFFERENTIATED PRICING OF PATENTED PRODUCTS (WHO, Commission on Macroeconomics and Health Working Paper No. 2, 2001).

⁶³ 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 61, at § 16.05[3]. The amendment was included as part of the Uruguay Round Agreements Act by which the U.S. joined the WTO. Uruguay Round Agreements Act, Pub. L. No. 103-465, 108 Stat. 4809

extent of the rejection may not yet be clear,⁶⁴ although the recent Free Trade Agreement with Australia commits both parties to the domestic exhaustion rule.⁶⁵

Even if the United States follows 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.⁶⁶ However, the Prescription Drug Marketing Act of 1987 blocks re-importation by anyone other than the manufacturer, forbidding this form of arbitrage.⁶⁷

2. National Drug Regulatory Agencies (NDRAs)

The TRIPS Agreement generally leaves the drug approval process to individual countries.⁶⁸ 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

(1994) (§ 533 of the Uruguay Round Agreements Act amended 35 U.S.C. §271(a) to expand the definition of infringement to include importation into the U.S. of a patented product). The legislative history of this provision is obscure. The House Reports on the Uruguay Round Agreements Act do not include an analysis of Section 533, and the only mention in the summary description is: "amends the definition of infringing activity to include offers for sale and importation of a patented good." H.R. Rep. No. 826(I), at 8. The unofficial summary by the Congressional Research Service merely states: "(Sec. 533) Deems offering to sell or import a patented invention into the United States to be patent infringement." Congressional Research Service, Bill Summary & Status, H.R. 5110 (Pub. L. No. 103-465), 103rd Cong., 2nd Sess. (summary dated Sept., 27, 1994).

⁶⁴ 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 ROTHNIE, *supra* note 57, at 183; Chisum, *supra* note 61, at §1605[3]. Second, it is not clear at all that Congress intended to overturn the international exhaustion exception by the enactment of § 533. One may declare importation an act of infringement, and yet retain the narrower exception for authorized sales abroad being imported legally under international exhaustion. But see Chisum, *supra* note 61, at §16.05[3]. Third, the provision, enacted as part of the Uruguay Round Agreements, was not required, as WTO Members retain domestic flexibility to choose any exhaustion rule. Finally, the heuristic of optimality (discussed in Section V *infra*) suggests that any provision which strengthens drug patent rights will enhance beneficial innovation only if patent rents were sub-optimal. This issue was not demonstrated to Congress in the legislative history to the 1994 amendment.

⁶⁵ In 2004, the U.S.-Australia Free Trade Agreement committed both parties to the domestic exhaustion rule for patents. U.S.-AUSTRALIA FREE TRADE AGREEMENT, § 17.9.4 (2004) available at www.ustr.gov.

⁶⁶ See Rebecca S. Eisenberg, The Shifting Functional Balance of Patents and Drug Regulation, 19 HEALTH AFF. 119, 129-32 (Sept./Oct. 2001). Re-imported patented drugs are produced in the U.S. 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 notes 63 and 64 *supra*. As we shall see in Section VII *infra*, Canadian pharmaceutical arbitrage has recently exploded despite this restriction.

⁶⁷ Prescription Drug Marketing Act of 1987, 21 U.S.C. §§ 331(t), 381(d) (2004).

⁶⁸ TRIPS Agreement, *supra* note 1, at art. 1, § 1.

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 impact the potential for product differentiation—an impediment to arbitrage—by allowing or disallowing certain marketing efforts and/or dictating transactions costs. For example, in 1997, the United States' national drug regulatory agency (NDRA), the Food and Drug Administration (FDA),⁶⁹ modified its regulations to permit direct to consumer (DTC) advertising for pharmaceutical drugs.⁷⁰ Virtually no other countries permit the practice.⁷¹ The creation of the DTC rule by the FDA modifies information costs related to substitution.⁷²

Other government regulations also influence pharmaceutical marketing. For example, federal law prohibits the sale of a drug sample⁷³ or the domestic resale of deeply-discounted drugs sold to certain hospitals,⁷⁴ 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.⁷⁵

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 Practice (GMP). PhRMA companies are now cooperating with the U.S., the E.U. and Japan to develop a higher global standard, known as the

⁶⁹ 21 U.S.C. § 355 (2004).

⁷⁰ The regulations are now found at 21 C.F.R. § 202.1 (2004).

⁷¹ In recent years, only the United States and New Zealand permit DTC broadcast ads. NIHCM, *supra* note 54, at 16. In 2002, Canada permitted restricted DTC advertising, and is affected by spillover from American media. Canadian Institute for Health Information, DRUG EXPENDITURE IN CANADA: 1985-2002 41 (2003). In the 2004 U.S.-Australia Free Trade Agreement, web-based DTC advertising is permitted. U.S.-AUSTRALIA FREE TRADE AGREEMENT, Annex 2-C, ¶ 5 (2004) available at www.ustr.gov.


⁷² Philips, *supra* note 37, at 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 54, at 2 (DTC advertising increases consumer sales of patented pharmaceuticals); CBO, INCREASED COMPETITION, *supra* note 56, 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% thereafter. Stephen Heffler et al., *Health Spending Projections For 2002-2012*, HEALTH AFF. (Web Exclusive, Feb. 7, 2003) at nn. 24-26 and text accompanying **[SC: Correct BB form; see how we have cited web exclusives in the past]**. 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 (Sept./Oct. 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 54, at 2.

⁷³ 21 U.S.C. §§ 331(t), 353(d).

⁷⁴ Prescription Drug Marketing Act of 1987, 21 U.S.C. § 353(c)(3) (2004).

⁷⁵ Schneider, *supra* note 4, at 26-36 (review of False Claim Act litigation against drug companies, particularly involving marketing related fraud); Department of Health and Human Services, COMPLIANCE PROGRAM GUIDANCE FOR PHARMACEUTICAL MANUFACTURERS, 68 Fed. Reg. 23731, 23733-39 (May 5, 2003).

International Conference on Harmonization (ICH).⁷⁶ Imposition of ICH would discourage substitution of drugs manufactured by less-expensive non-OECD 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.⁷⁷

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,⁷⁸ 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.⁷⁹ 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 re-importation of a prescription drug by anyone other than the manufacturer.⁸⁰ The law was ostensibly intended to address safety concerns for the U.S. pharmaceutical supply chain,⁸¹ but its effect is to prevent international pharmaceutical arbitrage or parallel e.

Finally, PhRMA companies 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 pricing⁸² and rate setting.⁸³ In others, price regulation occurs when the government enters

⁷⁶ Graham Dukes, Interim Report of Task Force 5 WORKING GROUP ON ACCESS TO ESSENTIAL MEDICINES 32 (UN Millennium Project, Feb. 1, 2004).

⁷⁷ The United States' 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; Activists, Drug Firms Duel Over Use of Funds for Generic Combination Drugs in Africa*, 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.

⁷⁸ 21 U.S.C. §§ 360(i), 381(a) (2004).

⁷⁹ See *supra* Section VII.

⁸⁰ Prescription Drug Marketing Act of 1987, 21 U.S.C. §§ 331(t), 381(d) (2004).

⁸¹ H.R. Rep. No. 100-76, at 7 (1987).

⁸² 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, Oct. 2003) (discussing reference price systems in Germany, The Netherlands, and New Zealand).

⁸³ House of Commons, Examination of Witnesses (Jan. 23, 2002) (examination of Dr. John Patterson) (“Prices almost never go up on medicines in this country [England], as you saw from the report to Parliament in December. In brief, the PPRS is a scheme which caps profits and profitability in our industry at a level equivalent to the average return on capital of the FT 100.”). [AU: To facilitate our sourcechecking, what type of source is this? How did you access it? ED: speech from the House of Commons website] The U.S. effectively sets rates for government purchase of services from physicians and hospitals, but generally not for pharmaceuticals.

the market as a purchaser and acts with monopsony power.⁸⁴ 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.⁸⁵ 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.⁸⁶ While these cost-saving measures do not directly affect arbitrage, companies under real or perceived profit pressure may seek enhanced protection against arbitrage or free riding.

3. 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 appropriation rights. Under the Hatch-Waxman Act⁸⁷ and other legislation such as the Orphan Drug Act,⁸⁸ the FDA may grant additional exclusive marketing periods under an array of circumstances—for example, rewarding first-mover generic drugs,⁸⁹ certain drugs for uncommon conditions (so-called orphan drugs),⁹⁰ or compliance with social goals such as testing drugs for efficacy and safety on children.⁹¹ 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.⁹² PhRMA companies are maximizing their opportunities under these provisions.⁹³

⁸⁴ In the U.S., the recently-enacted Medicare Act disabled federal monopsony power in the purchase of outpatient prescription drugs under Medicare. Medicare Prescription Drug Improvement and Modernization Act of 2003, Pub. L. No. 108-173, § 301, 42 U.S.C. §1395 et seq. [§ 1808(c)(1)(C) of the SSA] (2004).

⁸⁵ CBO, Increased Competition, *supra* note 56, at xi.

⁸⁶ *See, e.g.*, W. Va. Stat. § § 30-5-12 (2004) (allowing pharmacists to substitute generic medicines for brand name medicines without approval from the prescriber) and W. Va. Stat. §23-4-3 (2004) (requiring generic substitution within the Workers' Compensation program); *but see* Danzon & Ketcham, *supra* note 82, at 7 (Germany restricts generic substitution).

⁸⁷ 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 and 156 (2004).


⁸⁸ 21 U.S.C. §§ 360aa-360ee (2004).

⁸⁹ 21 U.S.C. § 355(j) (2004).

⁹⁰ 21 U.S.C. §§ 360aa-360ee (2004).

⁹¹ 21 U.S.C. § 355a (2004).

⁹² The term “exclusive marketing period” means the actual period during which a pharmaceutical company sells a FDA-approved drug in the United States without direct competition. The legal sources of this period include patent law, non-patent “exclusive marketing” rights granted by the FDA under Hatch-Waxman, the use of litigation and agreements to forestall competitive entry, and the ever-greening of patents through filings for new uses and formulations.

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  ess.⁹⁴ The U.S. is now exporting portions of the Hatch-Waxman Act to other countries through bilateral free trade agreements.⁹⁵

After a patent or exclusive marketing period expires,⁹⁶ 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.⁹⁷ These abuses prompted amendments to Hatch-Waxman in 2003.⁹⁸ PhRMA companies are already responding with new tactics keep generic drugs off the market by denying the generic companies an adequate financial return for the expensive generic approval process.⁹⁹

⁹³ For example, the number of putative orphan drugs qualifying for tax credits and extended exclusive marketing periods have soared as companies have narrowly defined markets to remain under the 200,000 person threshold. Steven R. Salbu, *AIDS and Drug Policy: In Search of a Policy*, 71 WASH. UNIV. L. Q. 691, 692, 704-06 (1993) (FDA designated AZT as an orphan drug in 1987; more than half of AIDS drugs as of August 31, 1991 were designated orphans); John J. Flynn, *The Orphan Drug Act: An Unconstitutional Exercise of the Patent Power*, 1992 UTAH L. REV. 389, 389-403 (FDA designated early AIDS drugs such as AZT, and other best-selling drugs such as EPO and Taxol as orphan drugs). The tax expenditure on the Orphan Drug Act is now \$200 million per year, not including the cost of the grant of market exclusivity. Joint Committee on Taxation, ESTIMATES OF FEDERAL TAX EXPENDITURES FOR FYS 2004-2008 (Joint Committee Print, Dec. 22, 2003). Public Citizen notes the inefficiency of the incentive mechanism: pediatric tests cost only \$3.9 million per drug on average, but the six-month patent extension can result in huge financial rewards exceeding \$1 billion. Public Citizen, THE OTHER DRUG WAR II: DRUG COMPANIES USE AND ARMY OF 623 LOBBYISTS TO KEEP PROFITS UP 4 (Public Citizen's Congress Watch, June 12, 2002). The FDA estimates the total cost of the pediatric testing initiative from 2001 to 2021 to be \$14 billion, approximately equal to the proposed 5 year AIDS program. U.S. Food and Drug Administration, THE PEDIATRIC EXCLUSIVITY PROVISION: STATUS REPORT TO CONGRESS (Jan. 2001).

⁹⁴ See, e.g., Elizabeth Stotland Weiswasser & Scott D. Danzis, *The Hatch-Waxman Act: History, Structure, and Legacy*, 71 ANTITRUST L. J. 585 (2003). Philipson and Mehoulan 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 & MEHOULAN, *supra* note 24, at 12 (emphasis in original).

⁹⁵ See, e.g., U.S.-AUSTRALIA FREE TRADE AGREEMENT, §17.9.6 (2004) available at www.ustr.gov.

⁹⁶ By the late 1990s, the U.S. pharmaceutical exclusive marketing period was approximately fourteen years. CBO, Increased Competition, *supra* note 56, 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.

⁹⁷ Federal Trade Commission, GENERIC DRUG ENTRY PRIOR TO PATENT EXPIRATION: AN FTC STUDY 13-23 (July 2002).

⁹⁸ Prescription Drug and Medicare Improvement Act of 2003, 21 U.S.C. § 355(j) and tit. IX (uncodified, Pub. L. No. 108-173), 117 Stat. 2448 (2004). The Congressional Research Service prepared a summary of the Act on June 13, 2003 which provides some guidance on Congress's intent in amending Hatch-Waxman. See Congressional Research Service, PRESCRIPTION DRUG AND MEDICARE IMPROVEMENT ACT OF 2003 (Bill Summary and Status, S.1, 108th Cong.) (June 13, 2003).

⁹⁹ Leila Abboud, *Drug Makers Use New Tactic to Ding Generics*, WALL ST. J., Jan. 27, 2004, at B1.

V. The Heuristic of Globally Optimal Patent Rents

A. 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 appropriation in order 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.¹⁰⁰ They call it “theft” or “piracy.” At best, nonrival users are characterized as “free riders” or “charity.” These terms are inappropriate. When a starving person takes some bread, something has been taken: the store now has less bread than it had before.¹⁰¹ When nonrival access is provided to pharmaceutical knowledge, nothing has been lost, so long as the socially optimal level of appropriation for R&D is still achieved. In a world of excessive appropriation, we should call it theft (or genocide) to deny nonrival access to low income populations.

Assume that for the pharmaceutical industry there is a globally optimal patent rent.¹⁰² The globally optimal patent rent must be sufficient to fund the socially 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 appropriation harms human health without advancing socially optimal R&D. Society must decide when the best level of appropriation has been reached.¹⁰³

Maximizing R&D at all costs should not be our objective. Resources devoted to R&D are not available for other uses.¹⁰⁴ Uwe Reinhardt puts it this way: “Year after year,

¹⁰⁰ DRAHOS, *supra* note 2, at 19-29 and *passim* (piracy); STERK, *supra* note 16, at 24-25 and *passim* (analogies to tangible property); and LEMLEY, *supra* note 16, at 3-16 (property and free riding).

¹⁰¹ Even this theft may be morally or economically defensible in some circumstances.

¹⁰² The economic analysis of socially optimal patents has been undertaken by Nordhaus and Scherer. Scherer, *Optimal Patent Life*, *supra* note 30, at 422; Nordhaus, *The Optimum Life of a Patent*, *supra* note 30, at 428; NORDHAUS, INVENTION, GROWTH & WELFARE, *supra* note 30, at ch. 5. Scherer argues that shortening patent life will reduce R&D only for the most marginal inventions, particularly in industries with nonpatent barriers to entry and post innovation pricing discipline. Scherer, *Optimal Patent Life*, *supra*, at 426. The pharmaceutical research industry contains both conditions. Nordhaus concluded that a fixed patent life was not optimal, but given that requirement, the length of the life should err to a longer rather than a shorter period. Nordhaus, *The Optimum Life of a Patent*, *supra* at 428. Philipson and Mechoulan cover the same territory when they argue that “[a]ppropriate policy must *simultaneously* solve the externality problem ex-post and the R&D problem ex-ante.” PHILIPSON & MECHOULAN, *supra* note 24, at 12-15. Recently, Christopher Yoo undertook a nuanced review of copyright law which covers some of the same terrain as my approach, but with assumptions of copyright market entry and substitutability which do not apply to pharmaceutical patents. See Christopher S. Yoo, *Copyright and Product Differentiation*, 79 NYU L. REV. 212 (2004).

¹⁰³ Philipson and Méchoulan 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 24, at 2.

¹⁰⁴ Currently the U.S. spends more than fifteen percent of its GDP on health care. Stephen Heffler et al., *Health Spending Projections Through 2013*, HEALTH AFF. exh. 1 (Web Exclusive, Feb. 11, 2004) [SC:

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.”¹⁰⁵

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,¹⁰⁶ and funds for neglected disease innovation are literally going to the dogs,¹⁰⁷ but malaria and AIDS vaccines are not available.¹⁰⁸

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 year¹⁰⁹ and Larry Lessig implores us not to allow IP law to be perverted while a holocaust devastates millions in the developing world.¹¹⁰ 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.”¹¹¹ In a major study, the Congressional Budget Office conceded that no one knew whether current levels of pharmaceutical R&D were optimal.¹¹² And yet this is the pressing question.

B. Globally Sub-Optimal Patent Rents

Correct BB form; see how we have cited web exclusives in the past; compare with footnote 64].

Perhaps we can agree that increasing pharmaceutical R&D to twenty percent or fifty percent of GDP would be excessive.

¹⁰⁵ Uwe E. Reinhardt, *An Information Infrastructure For the Pharmaceutical Market*, 23:1 HEALTH AFF. 107 (Jan/Feb 2004). [SC: Correct citation form]

¹⁰⁶ Viagra (sildenafil) was approved by the FDA in 1998, Levitra (vardenafil) in August 2003, and Cialis (tadalafil) in November 2003. See FDA TALK PAPER, FDA APPROVES THIRD DRUG TO TREAT ERECTILE DYSFUNCTION (Nov. 21, 2003), <http://www.fda.gov/bbs/topics/ANSWERS/2003/ANS01265.html>; 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>; FIRST ORAL THERAPY FOR ERECTILE DYSFUNCTION, 28 FDA Medical Bull. 1 (Summer 1998), available at <http://www.fda.gov/medbull/summer98/erectile.html>.

¹⁰⁷ In 1999, the FDA approved two drugs to treat canine Cognitive Dysfunction Syndrome, also known as separation anxiety in dogs. FDA TALK PAPER, FDA APPROVES FIRST BEHAVIORAL DRUGS FOR DOGS (Jan. 5, 1999), <http://www.fda.gov/bbs/topics/answers/ans00934.html>. Perhaps soon a drug will be developed for erectile dysfunction in dogs.

¹⁰⁸ For an introduction to donor efforts led by the Bill & Melinda Gates Foundation to stimulate development of a malaria vaccine, see <http://www.malariavaccine.org>.

¹⁰⁹ JAMES LOVE, STATEMENT OF ESSENTIAL INVENTIONS, INC. TO THE COMMISSION ON INTELLECTUAL PROPERTY RIGHTS, INNOVATION AND PUBLIC HEALTH, at 2, April 5, 2004.

¹¹⁰ Lawrence Lessig, *The International Information Society*, 24 Loy. L.A. Ent. L. Rev. 33, 36-37 (2004).

¹¹¹ JOSEPH A. DIMASI & HENRY G. GRABOWSKI, PATENTS AND R&D INCENTIVES: COMMENTS ON THE HUBBARD AND LOVE TRADE FRAMEWORK FOR FINANCING PHARMACEUTICAL R&D, at 2 (presentation, June 25, 2004). 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 24.

¹¹² 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 56, at 48.

Globally sub-optimal patent rents would stifle the production of pharmaceutical knowledge, creating a generational equity issue. The present group of patients may benefit from sub-optimal patent rents because innovative treatments are cheaper and more available, but future quality will be compromised. Pharmaceutical companies would invest less when creating inappropriable knowledge. This is the nightmare scenario portrayed by PhRMA companies when they articulate the fear that innovation may be squelched.

C. Globally Supra-Optimal Patent Rents

Globally supra-optimal patent rents are rarely recognized as a problem by PhRMA companies. By definition, supra-optimal patent rents are not required to fund innovation. Supra-optimal patent rents harm consumers by raising prices and restricting access without the counterbalancing benefits of future innovation.

1. Are Supra-Optimal Patent Rents Possible?

One economist reviewer of an earlier draft of this Article suggested that patent rents cannot be supra-optimal because PhRMA companies have not fully appropriated all consumer surplus associated with their products.¹¹³ This is another way of saying that PhRMA companies have not yet achieved first degree differential pricing (or Ramsey Optimal Pricing). Ramsey Optimal Pricing would maximize the sales and profits of PhRMA companies, but 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 patent 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 patent rents may be supra-optimal.

2. Are Patent Rents Supra-Optimal?

¹¹³ I thank Aidan Hollis for this comment.

Some empirical evidence suggests that PhRMA companies earn well above market rates of return, one possible indicator of supra-optimal patent rents.¹¹⁴ The industry's long-term profits are four times the rate of the Fortune 500.¹¹⁵ 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.¹¹⁶

Optimal patent 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.¹¹⁷

The ways in which PhRMA companies currently opt to spend their cash flows may also indicate the supra-optimality of patent rents. The pharmaceutical industry currently spends more on sales and marketing than on R&D.¹¹⁸ Large marketing expenses are not proof that pharmaceutical patent 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 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,¹¹⁹ suggest that the neo-classical link between patents and innovation is overstated, particularly for

¹¹⁴ 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, Hansen & Grabowski, *supra* note 23. IRS data shows extraordinary profits and low taxation, Gary Guenther, Congressional Research Service, Federal Taxation of the Drug Industry from 1990 to 1996 (Dec. 13, 1999), but is protected against public disclosure by the Internal Revenue Code. Accurate pricing data is unavailable outside of the companies. CBO, Increased Competition, *supra* note 56, at 20. On the theoretical front, useful questions are posed by Reinhardt, *supra* note 105; and William S. Comanor, *Political Economy of the Pharmaceutical Industry*, 24 J. ECON. LIT. 1178, 1182-86 (1986).

¹¹⁵ DAVID H. KRELING ET AL., PRESCRIPTION DRUG TRENDS: A CHARTBOOK UPDATE exh. 32 (The Kaiser Family Foundation, Nov. 2001). The judgment of the equity markets is significant, even under a weak form of the efficient capital markets hypothesis.

¹¹⁶ Guenther, *supra* note 114.

¹¹⁷ *Id.*

¹¹⁸ KRELING, *supra* note 115 at exh. 30 (top 10 major pharmaceutical manufactures in 2000 spent 34.4% of revenues on "marketing, general and administrative" and 13.7% on "research and development;" *but see* Uwe E. Reinhardt, *Perspectives on the Pharmaceutical Industry*, 20 HEALTH AFF. 136 (2001) (not all SG&A expenses are truly marketing). With deference to Reinhardt, the differential is large enough to suggest that R&D receives less than marketing, absent more specific and verifiable data.

¹¹⁹ The classic 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 (Winter/Spring 2003).

industries marked by cumulative innovation¹²⁰ such as genetics.¹²¹ If so, the optimal patent rent may be less 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.¹²² This fact alone is a compelling reason to demand transparency. It certainly seems plausible to presume that supra-optimal patent rents are currently being collected. The burden of coming forward with contrary evidence could be placed on the parties controlling the relevant information, the PhRMA companies.

D. Implications of Global Optimality

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

1. 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, with no markets actually lost to the pharmaceutical companies. These non-market patients could receive unlicensed or royalty-free drugs without impacting the cash flow of PhRMA companies. F.M. Scherer recently made a similar point when he argued for allowing free riding by developing countries on pharmaceutical patents.¹²³

If global patent rents are sub-optimal, royalty-free production should still be allowed so long as it did not replace any commercial market, and thus did no financial harm to the patent owner.¹²⁴

¹²⁰ 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.

¹²¹ The work of Tim Hubbard and Jamie Love is particularly interesting in this regard. Hubbard & Love, *supra* note 21.

¹²² See *supra* note 114. Pharmaceutical pricing and profitability data is 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 (“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.

¹²³ F.M. Scherer, *A Note on Global Welfare in Pharmaceutical Patenting*, 27 *The World Economy* 1127, 1141 (2004) [hereinafter Scherer, *Global Welfare*].

¹²⁴ Philipson and Mechoulan criticize this position, but their stance is undermined if global patent rents are supra-optimal. PHILIPSON & MECHOULAN, *supra* note 24, 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

If global patent rents are supra-optimal, PhRMA companies could also 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 patent rents were supra-optimal.

a. Nonrival Access Improves With the 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, compulsory licensing may be required.

Sovereign threats of compulsory licenses, public pressure from NGOs, and actual competition from unlicensed generic companies persuaded PhRMA companies and the U.S. to embrace significant ARV differential pricing for poor countries. Compulsory licensing creates a credible threat on the part of low and medium income countries, pressuring PhRMA companies to undertake the trouble of differential pricing. 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 programs.¹²⁵ PhRMA companies strongly resisted both significant price reductions as well as unlicensed ARV drugs, citing both TRIPS and domestic IP legislation.¹²⁶ In response to the high cost of ARVs in low income countries, Médecins sans Frontières and other NGOs flouted IP law and procured unlicensed ARVs.

Several examples illustrate the effectiveness of credible threats of unlicensed production without royalties. Brazilian threats of compulsory licenses, coupled with its pre-TRIPS absence of pharmaceutical patents, permitted the distribution of free ARVs within Brazil, achieving the gold standard of nonrival access.¹²⁷ In January 2001, the

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.

¹²⁵ MÉDECINS SANS FRONTIÈRES, SURMOUNTING CHALLENGES: PROCUREMENT OF ANTIRETROVIRAL MEDICINES IN LOW- AND MIDDLE INCOME COUNTRIES: THE EXPERIENCE OF MÉDECINS SANS FRONTIÈRES 7, 9, 42 (pre-publication draft, 2003) [hereinafter MSF, SURMOUNTING CHALLENGES] (report prepared by MSF at the request of the WHO); Marleen Boelaert et al., *Letter to the Editor*, 287 JAMA 840-41 (2002) (“This impressive discount offered by the companies to developing countries was not merely due to public outcry, but mostly as a response to competition by generic drugs.”).

¹²⁶ MSF, SURMOUNTING CHALLENGES, *supra* note 125; ‘t Hoen, *supra* note 7, at 30-33; Susan K. Sell, *TRIPS and the Access to Medicines Campaign*, 20 WISC. INT’L L. J. 481, at 491-96 (2002) [hereinafter Sell, *TRIPS*]; Judy Rein, *International Governance Through Trade Agreements: Patent Protection for Essential Medicines*, 21 NORTHWESTERN J. INT’L L. & BUS. 379, 394-404 (2001).

¹²⁷ Jorge Bermudez, *Expanding Access to Essential Medicines in Brazil: Recent Economic Regulation, Policy-Making and Lessons Learnt*, in THE ECONOMICS OF ESSENTIAL MEDICINES, *supra* note 3, at 193; U.K. COMM’N ON INTELLECTUAL PROPERTY RIGHTS, INTEGRATING INTELLECTUAL PROPERTY RIGHTS AND DEVELOPMENT POLICY 43 (Sept. 2002); *see also* Rein, *supra* note 126, at 394-404 (resistance by Brazil, South Africa and Thailand); Jerome H. Reichman with Catherine Hasenzahl, *Non-Voluntary Licensing of Patented Inventions: Historical Perspective, Legal Framework Under TRIPS, and an Overview of the*

United States requested a WTO panel against Brazil to prevent Brazilian exports of unlicensed AIDS drugs to Africa.¹²⁸ Under international pressure, the U.S. withdrew the panel request on June 25, 2001, in the months leading up to Doha.¹²⁹

Voluntary no-royalty licenses such as Merck's recent grant to South African-Indian company Thembalami Pharmaceuticals,¹³⁰ must be viewed in the context of South Africa's compulsory licensing law. South Africa passed a compulsory licensing law in 1997,¹³¹ and was promptly sued by PhRMA companies. The U.S. government suspended bilateral economic assistance to South Africa as punishment for defending the suit.¹³² The U.S. government and PhRMA companies relented under great pressure in April 2001, shortly before the Fourth WTO Ministerial Conference in Doha.¹³³ Even the United States has resorted to this tactic in recent years. Threats of compulsory licensing of ciprofloxacin were instrumental in securing a lower price from Bayer,¹³⁴ and compulsory licensing remains an important remedy in litigation.¹³⁵

Practice in Canada and the USA 2 (UNCTAD-ICTSD Project on IPRs and Sustainable Development, Issue Paper No. 5, June 2003).

¹²⁸ WORLD TRADE ORG., REQUEST FOR THE ESTABLISHMENT OF A PANEL BY THE UNITED STATES, BRAZIL MEASURES AFFECTING PATENT PROTECTION, WT/DS199/3 (Jan. 9, 2001). Executive Order 13155 had specifically reserved to the United States the right to seek such a panel. Exec. Order No. 13155, 65 Fed. Reg. 30521, 30522 (May 10, 2000) ("this order does not prohibit the United States Government from invoking the dispute settlement procedures of the World Trade Organization to examine whether any such law or policy is consistent with" TRIPS). For an overview of the Brazilian and South African situations by the Congressional Research Service, see JOHN R. THOMAS, HIV/AIDS DRUGS, PATENTS AND THE TRIPS AGREEMENT: ISSUES AND OPTIONS 13-17 (CRS Report for Congress, July 27, 2001) [hereinafter THOMAS, CRS REPORT]. [EE: Small caps for CRS?, global change]

¹²⁹ 't Hoen, *supra* note 7, at 38-47; Thomas, CRS Report, *supra* note 128, at 15; Carlos M. Correa, *Implications of the Doha Declaration on the TRIPS Agreement and Public Health*, at 2, n.6 (WHO, Health Economics and Drugs, EDM Series No. 12, June 2002) [hereinafter Correa, *Implications of Doha*].

¹³⁰ Press Release, Merck & Co., Inc., Grants License for HIV/AIDS Drug Efavirenz to South African Company, Thembalami Pharmaceuticals, July 14, 2004, <http://www.pressmethod.com/releasestorage/5003645.htm>.

¹³¹ Medicines and Related Substances Control Amendment Act No. 90 of 1997 (Republic of South Africa).

¹³² Omnibus Consolidated and Emergency Supplemental Appropriations Act, 1999, 112 Stat. 2681-153 (1999) (suspending appropriation of all bilateral economic assistance to South Africa, including AIDS/HIV programs, until steps are taken to repeal section 15(c) of South Africa's Medicines and Related Substances Control Amendment Act No. 90 of 1997). Many commentators have written about the case and the U.S. trade pressure exerted upon South Africa. See, e.g., 't Hoen, *supra* note 7, at 30-31; Lissett Ferreira, *Access to Affordable HIV/AIDS Drugs: The Human Rights Obligations of Multinational Pharmaceutical Corporations*, 71 FORDHAM L. REV. 1133, 1155 (2002); Rein, *supra* note 126, at 400-402. Doha paragraph 4 discourages Members from exerting bilateral pressure which hinders the exercise of TRIPS and Doha rights. Correa, *Implications of Doha*, *supra* note 129, at 12.

¹³³ Editorial, *South Africa's Moral Victory*, 357 THE LANCET 1303 (Apr. 28, 2001); Thomas, CRS Report, *supra* note 128, at 16.

¹³⁴ Jill Carroll & Ron Winslow, *Bayer Agrees to Slash Prices for Cipro Drug*, WALL ST. J., Oct. 25, 2001 ("The agreement comes after a high-stakes threat by Tommy Thompson, HHS secretary, to break Bayer's patent for Cipro if he didn't get the price he wanted."). The U.S. compulsory license statutes are 7 U.S.C. § 2404 (patents necessary for the nation's food supply), 17 U.S.C. § 115 (2004) (copyrights to certain musical works), 28 U.S.C. § 1498 (2004) (patents); 35 U.S.C. § 203 (patents developed through the use of government research funding under the Bayh-Dole Act); and 42 U.S.C. § 2183 (atomic energy). The U.S.

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 2004.¹³⁶ 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 (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 most voluntary differential pricing programs continue to price significantly above unlicensed generic levels,¹³⁷ a practice generally followed in the US after generic market entry.¹³⁸

At the Fourth WTO Ministerial Conference in Doha, WTO members agreed to the Doha Declaration as an interpretation of TRIPS.¹³⁹ The Doha Declaration allows WTO

compulsory license statutes do not contain the restrictions required by Article 31 of TRIPS. *See* TRIPS Agreement, *supra* note 1, at art. 31. For an authoritative review of U.S. and Canadian experience with compulsory licensure, *see* Reichman with Hasenzahl, *supra* note 127, at 19-22.

¹³⁵ MAKAN DELRAHIM, FORCING FIRMS TO SHARE THE SANDBOX: COMPULSORY LICENSING OF INTELLECTUAL PROPERTY RIGHTS AND ANTITRUST (Presentation by the Deputy Assistant Attorney General, Antitrust Division, U.S. Department of Justice, at the British Institute of International and Comparative Law, May 10, 2004).

¹³⁶ *See, e.g.*, 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. Letter from Eugene Schiff, Agua Buena, to Joseph Saba, Axios (Sept. 20, 2004) (on file with author and available at: Healthgap listserv archives). A five company group negotiated with 5 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.

¹³⁷ MÉDECINS SANS FRONTIÈRES, UNTANGLING THE WEB OF PRICE REDUCTIONS: A PRICING GUIDE FOR THE PURCHASE OF ARVs FOR DEVELOPING COUNTRIES (6th ed. April 19, 2004) available at: 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 unlicensed generic provider is Hetero of India, at US\$347 per year. *Id.* at 12, 22. Merck matches the unlicensed generic price only in Low Human Development Index (HDI) countries and Medium HDI countries with adult HIV prevalence of 1% 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 1%, such as Columbia.

¹³⁸ CBO, INCREASED COMPETITION, *supra* note 56, at xiii.

¹³⁹ *Doha Declaration on TRIPS*, *supra* note 27. The legal status of the Doha Declaration is discussed in James Thuo Gathii, *The Legal Status of the Doha Declaration on TRIPS and Public Health Under the Vienna Convention on the Law of Treaties*, 15 HARV. J.L. & TECH. 291 (2002) and by Correa, *Implications of Doha*, *supra* note 129, at 5. The legal status of the Cancun General Council Decision is a joint commitment by WTO Members to abide by its terms in good faith. 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

Members to take measures to “protect public health and, in particular, to promote access to medicines for all.”¹⁴⁰ WTO Members may compel licensure to protect public health, without limitation to AIDS or any particular disease.¹⁴¹

The TRIPS Agreement restricts compulsory licenses predominantly to domestic use, effectively preventing exports.¹⁴² 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.¹⁴³ Compulsory licenses are not useful to Malawi absent the opportunity to import from Brazil, India or South Africa. The ensuing debate was energetic, leading up to the Cancun WTO meeting in 2003.

Immediately prior to the Cancun meeting, on August 30, 2003, the U.S. conceded the point. Under the Cancun General Council Decision, the WTO now permits exports of compulsory licensed drugs to the poorest countries.¹⁴⁴ The Cancun General Council Decision also established a WTO notification process for cross-border compulsory licenses. The TRIPS Council must be notified, but WTO approval is not required.¹⁴⁵ In May 2004, Canada amended the Canadian Patent Law to permit compulsory licenses for certain drug exports to needy nations.¹⁴⁶ As of September 2004, no WTO Member has

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. World Trade Organization, Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health, WT/L/540 ¶11 (Decision of the General Council of 30 August 2003) [hereinafter Cancun General Council Decision]. *Doha Declaration on TRIPS*, *supra* note 27, at ¶ 7.

¹⁴⁰ TRIPS Agreement, *supra* note 1, at art. 31(f); *Doha Declaration on TRIPS*, *supra* note 27, at ¶ 4.

¹⁴¹ *Id.* at ¶ 5; ‘t Hoen, *supra* note 7, at 40-41.

¹⁴² TRIPS Agreement, *supra* note 1, at art. 31(f).

¹⁴³ See *Doha Declaration on TRIPS*, *supra* note 27, at ¶ 6.

¹⁴⁴ *Cancun General Council Decision*, *supra* note 139; EU, CANCEL, *supra* note 139.

¹⁴⁵ *Cancun General Council Decision*, *supra* note 139, at ¶ 2. Notice must be given to the WTO, but approval is not part of the process. EU, CANCEL, *supra* note 139.

¹⁴⁶ 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.* at Schedule 1. France and Norway have recently followed suit, Law. N. 2004-800 (Aug. 6, 2004), 18 Journal Officiel Aug. 7, 2004 (France); 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 (Norway) available at IP-Health (July 31, 2004) [hereinafter Norwegian Compulsory License Regulation]. Norway does not have a significant pharmaceutical sector, so the impact of the regulation is modest. *Id.* at ¶7 (official explanation of the regulation). Canada is more likely to actually export, but the Canadian law is more restrictive than the Norwegian. See Global Access to Treatment: Canada’s Bill C-9 and the Compulsory Licensing of Pharmaceuticals for Export to Countries in Need (July 2004) available at <http://www.aidslaw.ca/Maincontent/issues/cts/patent-amend/billC-9flyer300604.pdf>. The Norwegian regulations are much less restrictive.

notified the TRIPS Council,¹⁴⁷ even though many companies are apparently exporting unlicensed generics without bothering to comply with the Cancun procedure.¹⁴⁸

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.¹⁴⁹ Differential pricing should be extended to target populations in a larger group of countries. If patent rents are supra-optimal, loss of some elite markets will not harm innovation. Even if patent rents are sub-optimal, additional countries can receive differential pricing if they undertake serious measures to segment and protect the local elite OECD market.¹⁵⁰ As the AIDS epidemic expands in Eastern Europe and Central Asia, access must be expanded to regions beyond sub-Saharan Africa.

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.¹⁵¹ 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 taking full advantage of TRIPS flexibilities.¹⁵² Second, the TRIPS-plus offensive of the USTR and the "Special 301" reports from that same office are frequently used to bluster countries into modifying 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

¹⁴⁷ 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.

¹⁴⁸ See *infra* Section VI.

¹⁴⁹ 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. All but three least developed countries in Africa have already adopted pharmaceutical patents, many years prior to the 2016 deadline. THORPE, *supra* note 27, at 1.

¹⁵⁰ See Section V.D.3 *infra*.

¹⁵¹ THORPE, *supra* note 27, at 1.

¹⁵² 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); GENEVA DECLARATION ON THE FUTURE OF THE WORLD INTELLECTUAL PROPERTY ORGANIZATION, SEPT. 22, 2004 available at IP-Health Listserve, Sept. 21, 2004 ("The WIPO technical assistance programs must be fundamentally reformed.")

Production by a third party does not add any marginal cost to the innovator, and thus will not harm innovation.¹⁵³ If global patent rents are supra-optimal, then royalty levels on compulsory licenses may be zero without loss of innovation incentives. The burden of proof of sub-optimality should be on the innovator companies seeking a higher royalty, and the royalty rate in conditions of sub-optimality should balance innovation and access goals.

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.¹⁵⁴ Second-degree price discrimination such as price controls or other domestic rules affecting appropriation also raise global coordination issues, which are now being negotiated in U.S. bilateral free trade agreements.¹⁵⁵

In all cases, such nonrival use by low income populations should be viewed as an opportunity rather than a problem.¹⁵⁶

2. Dysfunctional Pharmaceutical Arbitrage

The form of pharmaceutical arbitrage which is most likely to reduce appropriation is diversion from charitable non-commercial markets into high income markets.¹⁵⁷ If global patent 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.¹⁵⁸

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

¹⁵³ Assuming that production for compulsory licensure is limited to non-commercial markets. This result holds without regard for whether patent rents are currently super- or sub-optimal. Critiques of compulsory licenses by Merges and others are not applicable here because the goal is not the initiation of efficient bargaining around a rule, but the provision of essential medicines at marginal cost without harming innovation. See Robert P. Merges, *Contracting into Liability Rules: Intellectual Property Rights and Collective Rights Organizations*, 84 CALIF. L. REV. 1293 (1996) (arguing that compulsory licenses in digital media are less efficient than private contractual efforts).

¹⁵⁴ Particularly amongst the OECD, where free riding has the greatest potential to affect global patent rents. See Section V.D.7 *infra*.

¹⁵⁵ 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 (AUSTRALIAN NATIONAL UNIVERSITY INFORMAL WORKING PAPER, SEPT. 2004) (on file with author).

¹⁵⁶ Scherer, *Global Welfare*, *supra* note 123, at 1141.

¹⁵⁷ Parallel trade from poor countries to rich countries is incompatible with differential pricing of essential medicines. See DANZON & TOWSE, *supra* note 12 (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).

¹⁵⁸ DG Trade, *supra* note 36, at §1.

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.¹⁵⁹

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.¹⁶⁰ Even if the patients are market participants, receiving familiar medications from home, in their native language, might well be the best medical practice. In the U.S., uniform use of English labels in multicultural world 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 patent rents are supra-optimal. Put another way, parallel trade in patented pharmaceuticals within high income markets may be permitted. Pharmaceutical arbitrage within high income markets is the subject of Section VII below on Canadian-U.S. pharmaceutical arbitrage. If patent rents are sub-optimal, the domestic exhaustion rule should apply in high income markets, forbidding parallel imports into such countries and raising patent 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.

3. 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

¹⁵⁹ 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.

¹⁶⁰ Dukes, *supra* note 76, at 50, n.1. For more details on this case, *see infra* notes 307- 317 and text accompanying.

Argentina, these markets are significant and growing.¹⁶¹ The elites in low 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.¹⁶²

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 the markets,¹⁶³ much as they do in the U.S.¹⁶⁴ The persistence of domestic differential pricing, even in

¹⁶¹ In its 2001 submission to the United States Trade Representative, PhRMA claimed that \$260 million was lost annually due to unlicensed drug products in Argentina. Sell, *TRIPS supra* note 126, at n.55 (citing PHARM. RESEARCH MFRS. OF AM., NATIONAL TRADE ESTIMATE REPORT ON FOREIGN TRADE BARRIERS (NTE) (Dec. 17, 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. UNITED STATES OFFICE OF TRADE REPRESENTATIVE, 2003 NATIONAL TRADE ESTIMATE REPORT ON FOREIGN TRADE BARRIERS, ARGENTINA 6 (2003), available at http://www.ustr.gov/assets/Document_Library/Reports_Publications/2003/2003_NTE_Report/asset_upload_file997_6178.pdf. The estimate was dropped from the 2004 National Trade Estimate Report. UNITED STATES OFFICE OF TRADE REPRESENTATIVE, 2004 NATIONAL TRADE ESTIMATE REPORT ON FOREIGN TRADE BARRIERS, ARGENTINA (2004), available at http://www.ustr.gov/assets/Document_Library/Reports_Publications/2004/2004_National_Trade_Estimate_Report/asset_upload_file568_4735.pdf.

¹⁶² Pharmaceutical companies may currently prefer to keep the small full-priced elite market in developing countries rather than risk arbitrage. Oxfam, *Fatal Side Effects: Medicine Patents Under the Microscope*, in THE ECONOMICS OF ESSENTIAL MEDICINES, *supra* note 3, at 93 (drug companies target elite households in Argentina, Brazil, India and China); W. Duncan Reekie, *The Development Trilemma and the South African Response*, in THE ECONOMICS OF ESSENTIAL MEDICINES, *supra* note 3, at 161, 167 (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 Org.-World Trade Org., *Differential Pricing and the Financing of Essential Drugs*, in THE ECONOMICS OF ESSENTIAL MEDICINES, *supra* note 3, at 209, 213, 220 (recognizing elite drug markets in developing nations); FREDERICK M. SCHERER & JAYASHREE WATAL, POST-TRIPS OPTIONS FOR ACCESS TO PATENTED MEDICINES FOR DEVELOPING COUNTRIES (WHO Commission on Macroeconomics and Health, 2001) [hereinafter Scherer & Watal, *Post-TRIPS Options*]; PATRICIA DANZON & MICHAEL FURUKAWA, PRICES AND AVAILABILITY OF PHARMACEUTICALS: EVIDENCE FROM NINE COUNTRIES exh. 8 (undated presentation, on file with author) available at <http://hc.wharton.upenn.edu/danzon/index.htm> (prices normalized by national income in Chile and Mexico are 528% and 529% of the U.S. prices; I interpret this data to mean that drug purchasers in Chile and Mexico must have personal incomes far in excess of the national average). In their public filings with the U.S. Securities and Exchange Commission, PhRMA companies acknowledge the growing middle class markets in the developing world. MERCK & CO, INC., FORM 10-K (filed with the SEC on Mar. 10, 2004) at 14. PhRMA companies have recognized the potential of these markets for some time. GERALD MOSSINGHOFF, 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).

¹⁶³ 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 125, 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 functioning.

¹⁶⁴ See REPORT OF THE WEST VIRGINIA PHARMACEUTICAL COST MANAGEMENT COUNCIL, REFERENCE PRICING COMMITTEE 2-3, APP. A-1, A-2 (SEPT. 10, 2004) (Shana Phares & Kevin Outtersson, Co-Chairs)

the face of extensive donor programs, testifies 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.¹⁶⁵

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.¹⁶⁶ 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. A menu of these legal structures was provided in Section IV *supra*. If global patent 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 will not suffer much lost profit if all sales of HIV products in every low and middle income country dropped to zero. GlaxoSmithKline, the largest participant in the HIV market, reports sales in three geographic regions: the U.S., 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 sales in 2003 were only £155 million,¹⁶⁷ in a year when gross profit was £17.2 billion and 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, particularly if elite markets in these countries remain commercial.

4. 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

(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) *available at* <http://www.wvc.state.wv.us/got/pharmacycouncil/default.cfm> [hereinafter WEST VIRGINIA REPORT].

¹⁶⁵ 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 (alleged diversion from discounted hospital markets to higher-priced secondary markets). An overview of the potential legal mechanisms is provided in Section IV *supra*.

¹⁶⁶ *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) dated April 5, 2004 *available at* HEALTHGAP (July 31, 2004) (on file with author) (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).

¹⁶⁷ GLAXOSMITHKLINE PLC, 2003 ANNUAL REPORT, Form 20-F, at 61-63,

by the United States' National Institutes of Health (NIH), and the orphan drug tax credit. Pull subsidies directly address the appropriation issue. They 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 vaccine¹⁶⁸ or antidotes to bioterrorism.¹⁶⁹

The heuristic suggests three implications. First, for drugs or conditions with sub-optimal patent rents, government intervention should increase patent rents towards optimal levels. For example, subsidies are essential for neglected diseases, where the target population cannot afford any commercial price for therapy. Second, subsidies can be limited to drugs with sub-optimal patent rents without harming innovation. Scarce subsidies should not be directed to drugs with strong commercial potential, but should be reserved for neglected diseases. Finally, for patented drugs with supra-optimal patent 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. Scherer and Watal have proposed expanding U.S. tax incentives for donating pharmaceuticals to poor countries,¹⁷⁰ but this additional push subsidy is warranted only if patent rents are sub-optimal. Likewise, the US Congress on September 23, 2004 authorized \$7.6 billion to extend the expiring R&D tax credit for another 18 months without targeting specific disease conditions.¹⁷¹ Proposals for indiscriminate tax credits are unsupported absent evidence of sub-optimality of global patent rents.

5. National Drug Regulation and WHO qualification

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,¹⁷² some estimates put the cost of duplicative NDRA processes within the EU at £500 million per year.¹⁷³ NDRA rules also delay the launch of

¹⁶⁸ Michael Kremer, *Pharmaceuticals and the Developing World*, 16 J. OF ECON. PERSP. 67, 82-85 (2002). For a recent example, see 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> [SC: Replace with precise URL].

¹⁶⁹ The Congressional Research Service indicates that “guaranteeing a market through contract authority” is an aspect of President Bush’s Project BioShield to develop bioterror countermeasures. Frank Gottron, Project Bioshield (CRS Report for Congress, RS21507) (July 23, 2003). The proposed size of the pull subsidy for bioterror countermeasures is \$5.593 billion through FY 2013. *Id.*

¹⁷⁰ SCHERER & WATAL, POST-TRIPS OPTIONS, *supra* note 162.

¹⁷¹ Working Families Tax Relief Act of 2004, H.R. 1308, 108th Cong. §301 (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.

¹⁷² Council Regulation 2309/93, O.J. (L 214) as amended by Commission Regulation 649/98 O.J. (L 88) 7.

¹⁷³ ROTHNIE, *supra* note 57, at 493-94 and sources cited therein.

innovative drugs in many countries.¹⁷⁴ A “reference” approval process would reduce duplicative costs and speed market entry of pharmaceuticals.¹⁷⁵

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 patently useful in many regions, with many different companies producing unlicensed ARVs under unknown conditions.¹⁷⁶ In the 2004 World Health Assembly, the U.S. pushed to remove the word “strengthening” from the WHO HIV/AIDS Resolution concerning prequalification.¹⁷⁷ The word was retained in the final document,¹⁷⁸ but the U.S. continues to marginalize the prequalification process in PEPFAR.¹⁷⁹ The United States also implicitly opposed reference approvals in various free trade agreements, on the grounds that the rights of data exclusivity must be protected.¹⁸⁰ The recent Free Trade Agreement (FTA) with Australia requires linkage

¹⁷⁴ 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, July 2003). This study collects data on launch delay, and concludes that in addition to difficulties with the drug approval process, many companies delay applications to enter some smaller markets due to fears of pharmaceutical arbitrage. If global patent rents are supra-optimal, this industry practice is reprehensible, as it voluntarily withholds important drugs from patients.

¹⁷⁵ Many NDRAs practice a form of reference approval when they require, as a condition of application for marketing approval, prior marketing approval in either the U.S., 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.

¹⁷⁶ AMFAR, TREAT ASIA SPECIAL REPORT: EXPANDED AVAILABILITY OF HIV/AIDS DRUGS IN ASIA CREATES URGENT NEED FOR TRAINED DOCTORS, at 4, July 2004, available at www.amfAR.org.

¹⁷⁷ Compare World Health Org., A57/A/Conf.Paper No. 3 Rev. 1, 20 May 2004, with Rev.2 (May 21, 2004).

¹⁷⁸ WORLD HEALTH ORG., FIFTY-SEVENTH WORLD HEALTH ASSEMBLY, SCALING UP TREATMENT AND CARE WITHIN A COORDINATED AND COMPREHENSIVE RESPONSE TO HIV/AIDS, WHA57.14 (May 22, 2004) at 3(3).

¹⁷⁹ Marilyn Chase, *Generic AIDS Pill Gets Acceptance*, WALL ST. J., July 2, 2004, at B3.

¹⁸⁰ 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 (May 2004) (on file with author) available at <http://www.accessmed-msf.org/documents/ftabriefingenglish.pdf> [hereinafter MSF, FREE TRADE AGREEMENTS]; DAVID VIVAS-EUGUI, QUAKER UNITED NATIONS OFFICE, REGIONAL AND BILATERAL AGREEMENTS AND A TRIPS-PLUS WORLD: THE FREE TRADE AREA OF THE AMERICAS (FTAA) 16-18 (2003) (on file with author) [hereinafter VIVAS-EUGUI, QUAKER UN OFFICE].

between drug approval and patent status for the first time, exporting a portion of Hatch-Waxman to Australia.¹⁸¹

Resources are also wasted in the generic entry process. NDRA should not require generic applicants to repeat any clinical studies without a clear benefit to public health.¹⁸² 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.¹⁸³ U.S. “TRIPS-plus” proposals¹⁸⁴ to extend data exclusivity to 5 or 10 years¹⁸⁵ will further increase costs and delay generic entry. If patent 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.

6. 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 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 is preferred over 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. Many high income country price control systems include generics in some fashion in the reference price.¹⁸⁶ The special case for government intervention in pharmaceutical prices

¹⁸¹ M. Kevin Outterson, *Free Trade in Pharmaceuticals*, 181 *Med. J. Aust.* 260-61 (Sept. 6, 2004); Ken J. Harvey, et al., *Will the Australia-United States Free Trade Agreement Undermine the Pharmaceutical Benefits Scheme?*, 181 *Med. J. Aust.* 256-259 (Sept. 6, 2004).

¹⁸² PhRMA companies withhold much of this data as trade secrets, or seeks ‘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.

¹⁸³ Watal reports a lag of about two years for unlicensed pharmaceuticals reverse-engineered in India. Jayashree Watal, *Pharmaceutical Patents, Prices and Welfare Losses: A Simulation Study of Policy Options for India under the WTO TRIPS Agreement*, 23 *WORLD ECON.* 733-52 (2000).

¹⁸⁴ “TRIPS Plus” refers to provisions which exceed the floors established under the TRIPS Agreement.

¹⁸⁵ MSF, *FREE TRADE AGREEMENTS*, *supra* note 180 at 4-6; OXFAM INT’L, *UNDERMINING ACCESS TO MEDICINES: COMPARISONS OF FIVE US FTA’S* 13-15 (OXFAM BRIEFING NOTE, JUNE 2004); VIVAS-EUGUI, QUAKER UN OFFICE, *supra* note 180, at 16-18. The U.S. is currently pressuring Israel to accept 5 to 10 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 (no page number available) available at 2004 WL 65711471; Hadas Manor, *US to Israel: Grant 5-Year Exclusivity for Ethical Drugs*, *Globes (Israel)* (no page number available) July 1, 2004 available at <http://www.globes.co.il/serveen/globes/docview.asp?did=810543&fid=942>.

¹⁸⁶ DANZON & KETCHAM, *supra* note 82, at 6-8 (Germany and The Netherlands); SARAH F. JAGGAR, *PRESCRIPTION DRUGS: SPENDING CONTROLS IN FOUR EUROPEAN COUNTRIES* 48-77 (GAO REPORT

derives from the monopoly market power granted by the state to patented drugs. Generic products do not generate monopoly rents, and thus should be exempt.¹⁸⁷

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.¹⁸⁸ 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 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 appropriation necessary to ensure optimal R&D. Any modifications to the strength of appropriation 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.

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 of existing therapies. In other

GAO/HEHS-94-30, MAY 1994) 48 (France, Germany, Sweden and the United Kingdom). Similar approaches are utilized in Australia. LOKUGE & FAUNCE, *supra* note 155, at 7-8; SANJOY ROY, AN OVERVIEW OF PHARMACEUTICAL REFERENCE PRICING AND REIMBURSEMENT: ANALYSIS OF THE AUSTRALIAN PHARMACEUTICAL BENEFITS SCHEME 2-11 (W.V. PHARMACEUTICAL COST MANAGEMENT COUNCIL, AUG. 2, 2004) available at: <http://www.wvc.state.wv.us/got/pharmacycouncil/default.cfm>.

¹⁸⁷ 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.

¹⁸⁸ F.M. Scherer & Jayashree Watal, *The Economics of TRIPS Options for Access to Medicines*, in THE 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 as 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 (also suggesting preventing parallel exports from any price-controlled country). Danzon and Towse address the external reference pricing problem by suggesting increased pricing obscurity and opacity so that the rock-bottom prices are not "directly observable." DANZON & TOWSE, *supra* note 12, at 6, 16-17. Their solution is vigorously rejected by Médecins sans Frontières, which has been very active in negotiations price discounts and distributing ARVs in sub-Saharan Africa. MSF, UNTANGLING THE WEB, *supra* note 137; MSF, SURMOUNTING CHALLENGES, *supra* note 125, at 7.

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.¹⁸⁹

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.¹⁹⁰

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 reimbursement, needlessly reinventing the wheel each time. These unnecessary costs raise the required patent rents without social benefit. The economic evaluation studies submitted to the Australian PBAC would be very helpful in formulary and reimbursement decisions worldwide.¹⁹¹ Further, if certain forms of price controls are adopted, optimizing patent 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.¹⁹² It strains credulity to base important pharmaceutical policy decisions on secret industry data, unavailable for study by other researchers.

7. 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.¹⁹³ Free riding by high income countries is a more complicated problem.

In the post-Bismark world, 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 should governments accept Ramsey Optimal Pricing based upon the government's ability to pay. Governmental resources are too scarce to completely neglect the monopsony power, with the possible (temporary) exception of the United States.¹⁹⁴

¹⁸⁹ LOKUGE & FAUNCE, *supra* note 155, at 7-8; SANJOY ROY, *supra* note 186, at 12-23.

¹⁹⁰ JAGGAR, *supra* note 186, at 69-77, JOAN-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).

¹⁹¹ Outtersson, *supra* note 181, at 260-61.

¹⁹² DiMasi, Hansen & Grabowski, *supra* note 23. 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

¹⁹³ Scherer, *Global Welfare*, *supra* note 123, at 1141.

¹⁹⁴ 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 (codified at § 1808(c)(1)(C) of the Social Security Act). However, the United States is not entirely immune to rate-setting inclinations in health care. Almost every other major health care good or

Acting solely in the national interest, governments may negotiate for the lowest possible prices, unconcerned about the possible negative global effects on innovation. PhRMA companies may respond by raising prices in uncontrolled markets. The U.S. is the largest such market. Put bluntly, high income countries with price controls are said to be free riders on American innovation.¹⁹⁵

Whether the free rider thesis is true empirically is an open question.¹⁹⁶ Perhaps the crusade against the scourge of low-priced drugs is misplaced. Perhaps American prices are supra-optimal and Canadian prices are optimal.¹⁹⁷ 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 U.S.¹⁹⁸ It may be unfair to label such countries as free riders. Empirical doubts are also raised when the U.S. 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.¹⁹⁹ 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. To answer these questions properly requires transparent research access to confidential company data. In any event, free riding is an innovation problem only if global patent rents are sub-optimal.

The current PhRMA company solution is to use U.S. free trade agreements to raise drug prices outside of the U.S.²⁰⁰ To this end, USTR recently created the post of

service purchased by Medicare or Medicaid is subject to rate-setting, including the services of physicians, hospitals, ambulatory surgical centers, and home health agencies.

¹⁹⁵ US Editorial, *Lower US Prices Through Higher International Prices*, 9 *Pharma Pricing & Reimbursement* 222 (Aug. 2004).

¹⁹⁶ Kevin Outterson, *Free Trade Against Free Riders*, 9 *Pharma Pricing & Reimbursement* 254-255 (Sept. 2004).

¹⁹⁷ 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.

¹⁹⁸ OECD Health Data 2004, table 14 (1st ed., June 3, 2004) *available at* http://www.oecd.org/document/16/0,2340,en_2825_495642_2085200_1_1_1_1,00.html (compared to the U.S., Canada, France, Germany, Switzerland and UK have higher total expenditures on pharmaceuticals as a percentage of total expenditure on health).

¹⁹⁹ WEST VIRGINIA REPORT, *supra* note 164, at App. A-2, A-2 (comparing Medicaid, private payor, 340b, Canadian, FSS and Australian data).

²⁰⁰ Elizabeth Becker & Robert Pear, *Trade Pact May Undercut Inexpensive Drug Imports*, N.Y. TIMES, July 12, 2004, at [SC: Insert page]; 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 *Brit. Med. J.* 1271-72 (2004); M.W. Serafini, *Drug Prices: A New Tack*, NAT'L J., Apr. 17, 2004, at 16 ("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."); M.W. Serafini, *The Other Drug War*, NAT'L J., Mar. 20, 2004, at 12; Elizabeth Becker, *Drug Industry Seeks to Sway Prices Overseas*, N.Y. TIMES, Nov. 27, 2003, at [SC: insert page]; Mark B. McClellan, Speech Before the First International

Assistant United States Trade Representative for Pharmaceutical Policy.²⁰¹ 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.²⁰² Small, poor countries offered a free trade deal with the U.S. may well agree to provisions which undermine health in order to serve commercial interests. Because these markets are small and generally poor, they 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 would 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.²⁰³ Other forms of global coordination should be considered, such as Jamie Love and Tim Hubbard's Global R&D Treaty.²⁰⁴ 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.

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.*, C. Bowe & G. 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.").

²⁰¹ A clear outline of the Bush Administration's pharmaceutical trade agenda can be found in the testimony of Grant D. Aldonas, Under Secretary of Commerce for International Trade, to the U.S. Senate Finance Committee on April 27, 2004. [SC: bluebook citation]

²⁰² 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 185 and text accompanying.

²⁰³ Aidan Hollis may well be the first to make this connection to counterfeiting explicit. AIDAN HOLLIS, AN EFFICIENT REWARD SYSTEM FOR PHARMACEUTICAL INNOVATION (July 2, 2004 draft) (prizes based upon therapeutic value) (unpublished manuscript on file with author) [hereinafter HOLLIS, EFFICIENT REWARD SYSTEM]. *See infra* Section VI.C.3 for a description of counterfeits.

²⁰⁴ 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, May 27, 2003); HUBBARD, *supra* note 13; LOVE, *supra* note 13.

8. Neglected and Global Diseases

a. Neglected Disease Innovation Does Not Require Expanded Appropriation in Low Income Countries

Jean Lanjouw and Professor Alan Sykes support the enactment of IP laws in low income countries to encourage the development of local markets for treating neglected diseases.²⁰⁵ 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),²⁰⁶ but those NCEs are either me-too generics or target global diseases.²⁰⁷ Sykes himself critiques Professor F.M. Scherer on the question of the net value of IP laws for developing countries. Sykes places his trust upon the huge disease burden in the developing world, which should stimulate markets if patents were available. Sykes thus looks to use IP laws to extract a greater portion of consumer surplus from the developing poor, in order to strengthen the incentives to innovate.²⁰⁸ Surely this is a last-ditch burden to impose on the world's poorest people, to be accepted only if all other solutions prove unworkable. We should not demand the widow's mite in order to fund PhRMA.

Strong IP laws in low income countries are not sufficient to create new markets for neglected disease drugs. If most patients in such countries are unable to purchase neglected disease drugs in commercial quantities and prices, the offer of patent protection will not stimulate R&D.²⁰⁹ An exclusive offer to sell drugs at a loss is not valuable.²¹⁰

²⁰⁵ Jean O. Lanjouw, A Patent Policy Proposal for Global Diseases 4 (June 11, 2001) (on file with author); Sykes, *supra* note 19, at 58-62.

²⁰⁶ JEAN O. LANJOUW, THE INTRODUCTION OF PHARMACEUTICAL PRODUCT PATENTS IN INDIA: 'HEARTLESS EXPLOITATION OF THE POOR AND SUFFERING?' (Nat'l Bureau of Econ. Research Working Paper No. 6366, Jan. 1998).

²⁰⁷ 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: DRIVING GROWTH 17-25 (Bear Stearns Healthcare Conference, Sept. 8, 2003) (on file with author) [hereinafter Levitt, Dr. Reddy's Laboratories]. The primary NDA filed by the company is amlodipine maleate, which is the salt version of an innovative drug, Norvasc. The NDA is being opposed in federal court by the innovator company. *Id.* at 20. Of the eight NCEs in the company's pipeline, seven will treat global diseases such as diabetes, cancer, metabolic disorders and cardiovascular disease. The eighth is an anti-infective drug, also for global diseases, but with more applicability in developing countries. *Id.* at 27. These are hardly the type of innovations that Lanjouw hoped for, and in fact this activity could hurt global innovation by reducing expected patent rents to innovator companies through early generic entry by aggressive Indian companies.

²⁰⁸ Sykes, *supra* note 19, at 61-62.

²⁰⁹ 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 & Co, Inc., Form 10-k (filed with the SEC on Mar.

Profit-maximizing Indian drug companies will focus on their best economic opportunities;²¹¹ neglected disease drugs are not be at the top of that list.²¹² The leading Indian drug companies derive most of their profits from sales in the U.S. and other high income markets.²¹³ 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.²¹⁴

Developing non-OECD 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

10, 2004) at 14 (“In recent years, the Company has been expanding its operations in countries located in Latin America, the Middle East, Africa, Eastern Europe and Asia Pacific where changes in government policies and economic conditions are making it possible for the Company to earn fair returns. Business in these developing areas, while sometimes less stable, offers important opportunities for growth over time.”).

²¹⁰ 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); Kettler & Modi, *supra* note 207, at 742 (Indian pharmaceutical companies will still require financial incentives to research and develop drugs for neglected diseases). A recent study of neglected vaccine projects found patent incentives to be completely ineffective. 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, Oct. 2003).

²¹¹ Kettler & Modi, *supra* note 207, 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 U.S. and Europe or branded (generic) formulations sold in India and other similar markets. Levitt, Dr. Reddy's Laboratories, *supra* note 207, at 9-10.

²¹² Jean O. Lanjouw and Iain Cockburn, *New Pills for Poor People?: Empirical Evidence After GATT*, 29 *WORLD DEV'T* 265-89 (2001) (their survey of Indian drug firms in 1998 found only 16% of their R&D targeted developing country markets). In fiscal year 2002-2003, Cipla's major innovative introduction was TIOVA, a long-acting bronchodilator for Chronic Obstructive Pulmonary Disease (COPD), a global disease. Cipla also launched a new generic ARV Fixed Dose Combination (FDC). CIPLA, SIXTY-SEVENTH ANNUAL REPORT 2002-2003 5 (available from the company and on file with author) [hereinafter CIPLA 2002-2003 ANNUAL REPORT].

²¹³ See, e.g., Rasul Bailay, *Cipla May Find Right Rx for Success: Indian Drug Firm Partners With Peers in U.S. to Crack No. 1 Market for Generics*, *WALL ST. J.*, Oct. 20, 2003, at A15; CIPLA 2002-2003 ANNUAL REPORT, *supra* note 212, at 7 (“During the year, Cipla's strategic alliances with leading generic companies in the USA and Europe were expanded to include additional products and projects. Currently, there are nearly 50 such projects in various stages of development in the USA alone.”). For Dr. Reddy's Laboratories, the U.S. market accounted for 57% of 2003 gross margin. Levitt, Dr. Reddy's Laboratories, *supra* note 207, at 11. **[ED: can you provide the materials from the MSF Malasian conference 2004?]**

²¹⁴ On PEPFAR procurement, see Section VI.C.4 *infra*.

countries, emerging companies may invest in regional markets heretofore overlooked by OECD companies,²¹⁵ and invest in process developments to lower production costs.²¹⁶

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,²¹⁷ attracting many commentators on the proper design of such a prize.²¹⁸ 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 U.S.), 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.

b. Global Disease Innovation Does Not Require Expanded Appropriation 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.²¹⁹ Global diseases²²⁰—

²¹⁵ 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 207, 17, *passim*; see also Kettler & Modi, *supra* note 207, at 743 (describing the Indian pharmaceutical industry).

²¹⁶ Kettler & Modi, *supra* note 207, at 743-45 (but Kettler and Modi do not assume an Indian comparative advantage in cost).

²¹⁷ 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* (Adam B. Jaffe, et al, eds., 2001) 35-109.

²¹⁸ See, e.g., HOLLIS, EFFICIENT REWARD SYSTEM, *supra* note 204; 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) (optional reward systems are superior to IP rights systems).

²¹⁹ Non-communicable disease accounts for forty-seven percent of the global burden of disease. 57th World Health Assembly, 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 Organization, World Health Report 2003. Stephen Leeder et al., A RACE AGAINST TIME: THE CHALLENGE OF CARDIOVASCULAR DISEASE IN DEVELOPING ECONOMIES 12-15 (2004) ("In 1998, non-communicable diseases were responsible for 59% of total global mortality and 43% of the global burden of disease. Importantly, 78% of [non-communicable disease] deaths were borne by low- and middle income countries, as was 85% of the NCD burden of disease...nearly 50% of deaths worldwide were due to CVD, diabetes, cancer and chronic lung disease."). PhRMA agrees with this position when it argues that the

conditions which affect patients in both rich and poor countries—include cancer and cardiovascular disease,²²¹ as well as AIDS.²²²

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)²²³ and two have been prequalified.²²⁴ These drugs are all related to treatment of AIDS and are off-patent in the United States.²²⁵ For the treatment of TB, the WHO prequalified non-licensed generic forms of patented ciprofloxacin from India and Spain.²²⁶ But these drugs may be used to

current ‘Western oriented’ R&D program actually includes diseases endemic to the entire world, such as cancer and CVD. Dukes, *supra* note 76, at App. 2, at 7-8 (Response of the Research-Based Pharmaceutical Industry to the Interim Report of the Task Force on Access to Essential Medicines) (Feb. 1, 2004).

²²⁰ 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 (Apr. 24, 2004).

²²¹ Carlos Correa interprets the *Doha Declaration* to include global diseases such as asthma and cancer. Correa, *Implications of Doha*, *supra* note 129, 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).

²²² North America and Western Europe account for less than 2 million of the 34 to 46 million people living with HIV/AIDS in 2003. UNAIDS/WHO, AIDS Epidemic Update 37 (2003) [hereinafter UNAIDS/WHO, AIDS Epidemic Update]. While AIDS is a global disease, at least 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 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: paediatric formulations are lacking and/or formulations do not meet children’s and caregivers’ needs (unpleasant tasting syrup, tablets too big to swallow, need to refrigerate some products, unbreakable tablets, lack of fixed dose combinations, and non-adapted dosages. For example there are currently no combinations for paediatric use”).

²²³ WHO, ACCESS TO HIV/AIDS DRUGS AND DIAGNOSTICS OF ACCEPTABLE QUALITY, PROCUREMENT QUALITY AND SOURCING PROJEC, 15TH ED., (May 27, 2004) [hereinafter, WHO HIV/AIDS Prequalification, 15th Ed.], available at <http://mednet3.who.int/prequal/> (last visited July 7, 2004).

²²⁴ Vinblastine and vincristine. WHO HIV/AIDS Prequalification, 15th Ed., *supra* note 223.

²²⁵ FDA Orange Book, available at: <http://www.fda.gov/cder/ob/default.htm> (visited Sept. 30, 2004).

²²⁶ WHO HIV/AIDS Prequalification, 15th Ed., *supra* note 223.

treat conditions other than TB and AIDS related cancers.²²⁷ The Doha Declaration was not limited to these three diseases, despite U.S. efforts to narrow the exception.²²⁸

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 U.S. negotiated to limit flexibilities to 22 diseases, keeping "lifestyle complaints and major western diseases" off the table.²²⁹ 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 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.²³⁰ Likewise, aggressive research programs are underway in 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 appropriation laws to encourage nonrival access, with substantial potential gains in global public health.

PART TWO: THE PRAXIS OF PHARMACEUTICAL ARBITRAGE

In Part Two 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 patent rents are supra-optimal or not, and whether one credits the safety of Canadian sourced drugs. If global patent rents are supra-optimal and safety concerns properly addressed, then U.S. consumers are needlessly overcharged for patented drugs, and many suffer negative health outcomes from restricted access.

²²⁷ 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.

²²⁸ 't Hoen, *supra* note 7, at 39-42; Correa, *Implications of Doha*, *supra* note 129, at vii, 15-16 (definition of emergency).

²²⁹ Roger Bate, *Entire IP System Could Easily Fall*, *Fin. Times* (London), Aug. 18, 2003, at 10.

²³⁰ Indeed, many early AIDS drugs qualified for orphan drug status in the U.S., when the expected U.S. market was fewer than 200,000 persons. Salbu, *supra* note 93, at 703-707.

VI. 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.

A. 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.²³¹ 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.²³² 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.²³³ Large scale roll-out of ARV therapy in low income countries is now a major global public health goal.²³⁴

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 U.S. is \$7215,²³⁵ and the recently introduced Fuzeon (enfuvirtide) costs \$20,000 per year.²³⁶ The

²³¹ UNAIDS/WHO, AIDS Epidemic Update, *supra* note 222, 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”).

²³² UNAIDS/WHO, AIDS Epidemic Update, *supra* note 222, at 38; Robert Greener, UNAIDS, *HIV/AIDS and Absorptive Capacity* (Kaiser Family Foundation HealthCast, Jan. 29, 2004) (2003 data) [hereinafter Greener, UNAIDS], available at http://www.kaisernet.org/health_cast/hcast_index.cfm?display=detail&hc=1066.

²³³ MSF, SURMOUNTING CHALLENGES, *supra* note 125, at 2, 5. Reuters, *UN To Seek \$6 Billion To Fight AIDS in Third World*, Nov. 6, 2003.

²³⁴ INST. OF MEDICINE, SCALING UP TREATMENT FOR THE GLOBAL AIDS PANDEMIC: CHALLENGES AND OPPORTUNITIES (July 2004); 57TH WORLD HEALTH ASSEMBLY, SCALING UP TREATMENT AND CARE WITHIN A COORDINATED AND COMPREHENSIVE RESPONSE TO HIV/AIDS, WHA57.14, May 22, 2004.

²³⁵ Calculation of the U.S. price comes from drugstore.com, at <http://www.drugstore.com> (60 tablets of Combivir for \$592.99, taken twice per day) (visited July 7, 2004).

²³⁶ Vanessa Fuhrmans, *Medical Dilemma: Costly New Drug for AIDS Means Some Go Without; Programs for the Uninsured are Facing Tough Choices With Advent of Fuzeon*, WALL ST. J., Jan. 13, 2004, at [SC: **Insert page**]. 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. U-WIRE, DUKE UNIVERSITY: NORTH CAROLINA FIRM’S NEW AIDS DRUG DEVELOPMENT ON HOLD, 2004 WL 59460572 (Jan. 22, 2004) (“Steve Sherman, director of North

annual per capita health expenditures in sub-Saharan Africa averages \$29.30²³⁷ and range from \$12 (Malawi) to \$253 (South Africa).²³⁸ 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.²³⁹ Indeed, for many patients, the drugs must be free. Recognizing the important public health issues, Brazil,²⁴⁰ India,²⁴¹ South Africa,²⁴² and China²⁴³ produce unlicensed 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.”²⁴⁴ Differential pricing is possible because of relatively low marginal costs of production. Most patented drugs can be produced relatively cheaply, absent research cost recovery. The primary variable expenses are direct manufacturing costs, which are a small fraction of the retail prices of patented ARVs. A high ratio of retail prices to direct manufacturing costs enables a company to sell at highly differentiated prices without selling below marginal cost.²⁴⁵

While the public does not know the true marginal manufacturing costs of most patented drugs, differential pricing and unlicensed generic production provides useful

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*.

²³⁷ WORLD BANK, 2004 WORLD DEVELOPMENT INDICATORS (2004) (citing 2001 data).

²³⁸ *Id.*; see also Markus Haacker, *Providing Health Care to HIV Patients in Southern Africa*, in THE 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).

²³⁹ 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 232. If these drugs were available at a much lower cost, resources could be redeployed to prevention and other unmet priorities.

²⁴⁰ ‘t Hoen, *supra* note 7, at 32-33.

²⁴¹ Mark Schoofs, *Clinton Program Would Help Poor Nations Get AIDS Drugs*, WALL ST. J., Oct. 23, 2003, at B1 (Indian and South African drug companies); CIPLA 2002-2003 ANNUAL REPORT, *supra* note 212, 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”).

²⁴² Schoofs, *supra* note 241, at B1 (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).

²⁴³ Jim Yardley, *China Begins Giving Free H.I.V./AIDS Drugs to the Poor*, N.Y. TIMES, Nov. 8, 2003, at A3.

²⁴⁴ DG Trade, *supra* note 36, at §2.2. Low income countries targeted for essential medications by the EU had a per capita income of less than \$765 in 2000.

²⁴⁵ SAGER & SOCOLAR, *supra* note 11, at 7 (roughly estimating marginal U.S. manufacturing and distribution costs for prescription drugs to be 9.9%).

proxies.²⁴⁶ 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 Combivir²⁴⁷ costs about \$19.76 per day or \$7215 per year by mail order in the United States.²⁴⁸ In sub-Saharan Africa in 2003, GlaxoSmithKline sells Combivir to health agencies at ninety cents per day or \$329 per year,²⁴⁹ and has announced a new non-profit price of sixty-five cents per day.²⁵⁰ Even this low price may not reflect GlaxoSmithKline's marginal cost, because Cipla sells an unlicensed generic form of Combivir to governments and nonprofit agencies at fifty-four cents per day or \$197.10 per year.²⁵¹ The differential pricing ratio for Combivir is approximately 35:1.²⁵² This ratio is likely to increase: MSF aims for an annual per patient cost of fifty to one hundred dollars in the near future.²⁵³ 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

²⁴⁶ Compulsory licensure enables ex-factory pricing closer to true marginal manufacturing cost, particularly if the tender process is competitive. Generic competition pierces the pricing veil, accelerates differential pricing towards true marginal production costs, and does not rely on public disclosure of confidential financial information from the companies. Given the endemic opacity of all PhRMA data on costs, perhaps the best way to calculate marginal cost is through compulsory licensure. PhRMA simply asserts that "there is no guarantee that generic companies will price at marginal cost." Dukes, *supra* note 76, App. 2, at 27 (Response of the Research-Based Pharmaceutical Industry to the Interim Report of the Task Force on Access to Essential Medicines) (Feb. 1, 2004). Absent the patent monopoly, generic companies in a competitive environment will certainly price much closer to marginal cost than PhRMA companies.

²⁴⁷ 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 137, at 13. The best clinical FDC also adds a NNRTI such as efavirenz (EFV). Gregory K. Robbins et al., *Comparison of Sequential Three-Drug Regimens as Initial Therapy for HIV-1 Infection*, 349 NEW ENG. J. MED. 2293 (Dec. 11, 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 (Dec. 11, 2003).

²⁴⁸ Calculation of the U.S. price comes from drugstore.com, at <http://www.drugstore.com> (60 tablets of Combivir for \$592.99, taken twice per day) (visited July 7, 2004).

²⁴⁸ 't Hoen, *supra* note 7, at 32-33.

²⁴⁹ MSF, UNTANGLING THE WEB, *supra* note 137, at 13.

²⁵⁰ GLAXOSMITHKLINE PLC, 2003 ANNUAL REPORT, Form 20-F, at 4, available at <http://www.sec.gov/edgar/searchedgar/companysearch.html>.

²⁵¹ MSF, UNTANGLING THE WEB, *supra* note 137, 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 250 at 29. Aspen's price is not yet listed in the pricing guide. MSF, UNTANGLING THE WEB, *supra* note 137, at 15.

²⁵² The numerator is \$7215 and the denominator is \$204.

²⁵³ MSF, SURMOUNTING CHALLENGES, *supra* note 125, at 9. As of 2004, the WHO 3 x 5 program estimates the per person per year cost for first-line drugs at U.S.\$304. WORLD HEALTH ORG., THE WORLD HEALTH REPORT 2004: CHANGING HISTORY 30 (2004).

you're electing to spend \$600, that means you're treating one person when you could be treating three."²⁵⁴

Triomune is Cipla's brand name for the most important triple-drug therapy FDC for sub-Saharan Africa, containing nevirapine (NVP), stavudine (d4T) and lamivudine (3TC). Triomune is produced as an unlicensed generic by Cipla Ltd and sold for sixty-seven cents per day or US\$ 244 per year.²⁵⁵ As of July 2004, Triomune is not available in a licensed form, a rare inversion in which a generic is a sole-source supplier.²⁵⁶ The patents for nevirapine, stavudine and lamivudine are held by different companies,²⁵⁷ 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 U.S., a ratio exceeding 46:1.²⁵⁸

High differential pricing ratios are not limited to ARVs. Ciprofloxacin is available in unlicensed generic form in Africa at \$0.0189 per 500 mg tablet,²⁵⁹ in the U.S. retail market it sells for about five dollars a pill,²⁶⁰ a ratio of 264:1. A high ratio is not necessarily a bad thing; in fact, if non-rival access is truly provided to the world's poorest communities, one would expect to find very large differential pricing ratios.

B. 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.²⁶¹ This article has been

²⁵⁴ 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).

²⁵⁵ MSF, UNTANGLING THE WEB, *supra* note 137, at 15.

²⁵⁶ UNICEF-UNAIDS-MSF, SOURCES AND PRICES OF SELECTED MEDICINES AND DIAGNOSTICS FOR PEOPLE LIVING WITH HIV/AIDS 18 (WHO/EDM/PAR/2004.4) (JUNE 2004) (NVP + d4T + 3TC fixed dose combination not available in the US).

²⁵⁷ FDA Orange Book, <http://www.fda.gov/cder/ob/default.htm> (visited Sept. 30, 2004). [detail]

²⁵⁸ 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 in U.S. \$, taken from www.drugstore.com, visited July 8, 2004. The ratio numerator is \$936 and the denominator is \$20.

²⁵⁹ World Health Org., International Drug Price Indicator Guide, <http://erc.msh.org/dmpguide/> (visited July 8, 2004).

²⁶⁰ Drugstore.com, at <http://www.drugstore.com> (visited July 8, 2004).

²⁶¹ 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 received for the next volume of the journal. Boelaert et al., *supra* note 125, 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

widely interpreted to claim that patents do not hinder ARV access in sub-Saharan Africa.²⁶² Attaran published a follow-on report in *Health Affairs* in 2004, again suggesting that patents have not been the major hindrance to ARV access.²⁶³ 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.²⁶⁴ As recently as 2002, no person in the developing world had received ARVs through official donor support from any country or multilateral institution.²⁶⁵ When MSF and Paul Farmer independently began proof of concept 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.²⁶⁶ Access to AIDS medications was discussed at the highest levels at the WHO as early as 1991,²⁶⁷ and at the International AIDS Conference in Durban in 2000.²⁶⁸ Thirteen years later, in 2004, the world is just beginning to scale-up towards 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

exist, other alternatives can be pursued, such as voluntary licensure or switching to another therapy. Where patents do not exist, they call for unlicensed production, ignoring the industrial infrastructure issue described above. Amir Attaran & Lee Gillespie-White, *In Reply*, 287 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).

²⁶² Lanjouw, Intellectual Property, *supra* note 62, at 11-12 (“industry uses this fact [the Attaran & Gillespie-White study] to stress that patents in the poorest countries are not impeding access to drugs”); *see, e.g.*, Harvey E. Bale, Jr., *Patents, Patients and Developing Countries: Access, Innovation and the Political Dimensions of Trade Policy*, in THE ECONOMICS OF ESSENTIAL MEDICINES, *supra* note 3, at 100, 106, n.10. Bale is the head of the international PhRMA company trade association.

²⁶³ Amir Attaran, *How Do Patents and Economic Policies Affect Access to Essential Medicines In Developing Countries?*, 23 Health Affairs 155, 156 (2004) (“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.”).

²⁶⁴ Combination therapy was available in the U.S. from December 1995 with 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 U.S. 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 (“Equatorial Africans faced death on the scale of the Holocaust”) (citing Dr. Don Francis, CDC AIDS Research, June 1984) (1988).

²⁶⁵ *African HIV/AIDS Crisis: Pursuing Both Treatment and Prevention: Hearing Before the Sen. Comm. on Foreign Relations, Subcomm. on African Affairs*, [107th Cong., 1st Sess.] (Feb. 14, 2002) (statement of Jeffrey D. Sachs). [SC: Bluebook]

²⁶⁶ 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*].

²⁶⁷ Gellman, *Unequal Calculus* *supra* note 266, at A1.

²⁶⁸ Esther Kaplan, *Time’s Up*, The Nation, July 22, 2004 (“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.”)

developing world, and they were too expensive because of patent protection and fears of arbitrage.²⁶⁹ Millions 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.²⁷⁰ In 2004, only one company produces unlicensed ARVs in Africa, Aspen Pharmacare in South Africa²⁷¹ (By contrast, Asia has twenty-seven companies producing unlicensed ARVs in eight countries.)²⁷² Attaran finds Aspen's home market, South Africa, to be effectively covered by patent filings. Indeed, PhRMA companies sued South Africa over unlicensed production of ARVs, as discussed in Section V.D.1 *supra*.

With South Africa stymied, unlicensed ARVs would have to be imported into sub-Saharan Africa from elsewhere, such as Brazil or India. Brazil was sued to block this practice,²⁷³ and India has faced a U.S.-requested WTO dispute resolution on its implementation of TRIPS for pharmaceuticals,²⁷⁴ as well as U.S. "Special 301" threats.²⁷⁵ The USTR frequently used the Special 301 watch list to discipline countries attempting to produce generics, even if legal under domestic law or TRIPS.²⁷⁶

The mere possibility of a patent filing acts as a deterrent to a generic new drug application in sub-Saharan Africa, since the innovator could undercut the market investment by the generic company, while tying them up in litigation. A recent study finds that all but three of Africa's least developed countries have implemented laws for pharmaceutical patents as of 2004, despite the flexibility granted by the Doha Declaration

²⁶⁹ JOAN-RAMON BORRELL AND JAYASHREE WATAL, IMPACT OF PATENTS ON ACCESS TO HIV/AIDS DRUGS IN DEVELOPING COUNTRIES (Center for Int'l Development, Harvard Univ., CID Working Paper No.92, May 2002) (Finding a significant increase in ARV uptake would have resulted absent patents; this paper is a static analysis, ignoring the innovation question, and does not model subsidized ARV markets, which might have demonstrated a much larger negative impact of patents). 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 profits in rich ones.").

²⁷⁰ Correa, *Implications of Doha*, *supra* note 129, at Annex 2.

²⁷¹ 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, a pharmaceutical plant was commissioned to produce ARVs factory in Nigeria, owned by Archy Pharmaceuticals Limited. Godwin Haruna, *First HIV/AIDS Drug Plant Takes Off*, This Day (Lagos), July 28, 2004 available at <http://allafrica.com/stories/200407280351.html>.

²⁷² AMFAR, *supra* note 176, at 4.

²⁷³ See *supra* notes 128 - 129 and text accompanying.

²⁷⁴ WORLD TRADE ORG., INDIA-PATENT PROTECTION FOR PHARMACEUTICAL AND AGRICULTURAL CHEMICAL PRODUCTS, WT/DS50/R (Sept. 5, 1997) and WT/DS50/AB/R (Dec. 19, 1997).

²⁷⁵ UNITED STATES OFFICE OF TRADE REPRESENTATIVE, 2004 SPECIAL 301 REPORT, available at: http://www.ustr.gov/assets/Document_Library/Reports_Publications/2004/2004_Special_301/asset_upload_file16_5995.pdf.

²⁷⁶ Sell, *TRIPS*, *supra* note 126, at 492.

to delay implementation until 2016.²⁷⁷ The attacks on Brazil, South Africa, and India were prominent and the intended lessons were not lost on other developing countries.

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,²⁷⁸ countries completely covered by TRIPS.²⁷⁹ USTR and PEPFAR also hinder procurement of unlicensed ARVs by multilateral and official donors, as discussed in Section VI.C.4 *infra*.

The patent thicket effectively covers all sources of unlicensed 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 unlicensed ARVs occurs by either complying with TRIPS flexibilities, or by (temporary) forbearance by the U.S. Perhaps Attaran and Gillespie-White should say that patent law shouldn't 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 didn't matter over the last decade for access to cheap ARV therapy in Africa.

C. Achieving Both Nonrival Access and Optimal Innovation

The next few pages present my proposals for maximizing public health while optimizing innovation. 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, the President's Emergency Plan For HIV/AIDS Relief (PEPFAR) is critiqued, particularly for its procurement and supply chain policies which are based upon a fear of pharmaceutical arbitrage.

1. 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.²⁸⁰ 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).²⁸¹ Requirements like these raise transaction costs and may allow pharmaceutical companies to delay the process for many months or

²⁷⁷ THORPE, *supra* note 27, at 1.

²⁷⁸ WHO, HIV/AIDS Prequalification, 15th Ed., *supra* note 223.

²⁷⁹ See *supra* notes 139 - 152 and text accompanying.

²⁸⁰ See, e.g., Norwegian Compulsory License Regulation, *supra* note 146, at §108; Canadian Bill C-9, *supra* note 146, at §21.04 (3)(d)(i)(B).

²⁸¹ Canadian Bill C-9, *supra* note 146, at §21.04 (3)(c)(i).

years. This process is wasteful, particularly when duplicated in multiple countries.²⁸² Good faith negotiations are not required in two circumstances: public non-commercial use, and “national emergency or other circumstances of extreme urgency.”²⁸³ 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 AIDS deaths in low and middle income countries now number in the millions. The process must be simpler and faster for nonrival access to medicines.

Critics state that no compulsory license has been issued under TRIPS.²⁸⁴ More precisely, no compulsory license has been issued under the Cancun General Council Decision, for several countries have issued TRIPS-compliant compulsory licenses without making the Cancun notification. Malaysia issued a compulsory license to Cipla Ltd. in February 2004 for importation.²⁸⁵ As of May 2004, compulsory licenses have also been issued by Cameroon, Mozambique and the Philippines.²⁸⁶ None of these have been posted on the WTO website as of October 2004, as required by Cancun.

Yet a singular focus on formal compulsory licenses for export under Cancun misses the point. Many companies are engaged in cross-border sales of unlicensed ARVs without complying with the Cancun process. Triomune is the best triple-drug FDC first-line treatment available in sub-Saharan Africa, and it is produced without a Cancun license. Brazil produces ARVs without license, both for domestic purposes and for aid projects to Africa. Thailand avoided a compulsory license by ruling Bristol-Myers’ didanosine patent invalid on public health grounds.²⁸⁷ All of these are proceeding informally, without complying with the Cancun procedure. Most are not prequalified by the WHO.²⁸⁸

PhRMA companies are demonstrating more pricing flexibility in 2004,²⁸⁹ particularly in first-line ARVs which enjoy significant unlicensed production.²⁹⁰ Second-line ARVs are a different story. No FDC containing efavirenz (EFV) is currently

²⁸² Blustein & Gellman, *supra* note 136.

²⁸³ TRIPS Agreement, *supra* note 1, Art. 31(b).

²⁸⁴ Amir Attaran, *Pharmaceutical Products, TRIPS, and the Doha Round: What are the Stakes?* slide 3 (Presentation at the American Enterprise Institute Conference, Sept. 2, 2003) available at http://www.aei.org/events/filter_eventID.605/summary.asp (visited Sept. 30, 2004).

²⁸⁵ *Cipla Gets Malaysian Nod for AIDS Drugs: In a Trailblazing Move, Malaysia Has Issued a Compulsory License*, BUSINESS STANDARD, 26 February 2004.

²⁸⁶ Statement of the Representative of Brazil, speaking on behalf of the GRULAC countries, at the WHO Executive Board Meeting, May 25, 2004 *quoted in* IP-Health (May 26, 2004).

²⁸⁷ *Government Pharmaceutical Organization v. Bristol-Myers*, Thailand Central Intellectual Property Court, Oct. 2002.

²⁸⁸ The amfAR July 2004 report notes the difficulties with twenty-seven companies in eight countries in Asia producing unlicensed ARVs, and only one of them (Cipla Ltd.) operating with WHO Prequalification. AMFAR, *supra* note 176, at 4.

²⁸⁹ *See, e.g.*, Press Release, Merck & Co., *supra* note 130.

²⁹⁰ MSF, UNTANGLING THE WEB, *supra* note 137, at 5-7.

available.²⁹¹ The USTR keeps the pressure on source countries under the Special 301 process. India and Thailand are major sources of FDCs for export, and both are under pressure from the USTR.²⁹² The U.S. and Thailand are negotiating a free trade agreement with TRIPS-plus provisions.²⁹³ Thailand is now preparing a generic FDC as a second-line therapy, containing efavirenz (EFV), lopinavir (LPV) and ritonavir (r), a protease inhibitor. The medical need for 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. This market should come in from the grey.

2. 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 Combivir²⁹⁴ is about \$20,000 in the U.S., but sells for as little as \$612 in Hyderabad and sub-Saharan Africa.²⁹⁵ 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 entrepreneurs²⁹⁶ will divert these drugs from the poor and export them to wealthy countries where they will fetch higher prices. Domestic arbitrage occurs within the U.S. at much lower thresholds, as demonstrated in Section VII.A *infra*.²⁹⁷ Since the great majority of the world's AIDS patients are in poorer countries, if only a small

²⁹¹ MSF, UNTANGLING THE WEB, *supra* note 137, at 6.

²⁹² USTR, 2004 National Trade Estimate Report on Foreign Trade Barriers, 217-220 (India), 463-465 (Thailand).

²⁹³ See the Thai Free Trade Agreement Watch website, www.ftawatch.org. See also Marwaan Macan-Markar, *Thailand-U.S.: Freer Trade Weakens Access to HIV/AIDS Drugs*, Inter Press Service News Agency, (May 21, 2004) available at <http://www.ipsnews.net/africa/interna.asp?idnews=23849> (visited Sept. 30, 2004).

²⁹⁴ 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 (total of all HIV sales), available at <http://www.sec.gov/edgar/searchedgar/companysearch.html>.

²⁹⁵ 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 <http://www.drugstore.com> (visited July 9, 2004).

²⁹⁶ Or smugglers, depending upon your perspective.

²⁹⁷ Jackie Judd, Senior Fellow with the Kaiser Family Foundation Speaks with Gilbert M. Gaul and Mary Pat Flaherty, Washington Post Staff Writers on a Five-Day Special Report Called "Pharmaceutical Roulette," that Focuses on Prescription Drug Safety Issues in the United States, (Kaiser Family Foundation transcript, Oct. 24, 2003), <http://www.kff.org> (describing significant arbitrage diversion within the U.S. market taking advantage of relatively modest price differentials).

percentage was diverted, significant volumes of ARVs could flow into high income country markets.²⁹⁸

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 \$25,000,²⁹⁹ comparable to the U.S. retail value of a kilogram of the active ingredients in Combivir.³⁰⁰ The U.S. retail price of a gram of cocaine is about \$100.³⁰¹ The retail price of cocaine in Columbia is between three dollars and five dollars per gram,³⁰² yielding a ratio of about 25:1.³⁰³ 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.³⁰⁴

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.³⁰⁵ 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.”³⁰⁶ Only six months later, GlaxoSmithKline, the patent holder for several important AIDS drugs, brought the sensational charge that 36000 packages of HIV/AIDS medicines worth approximately

²⁹⁸ 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 may not as price sensitive. DG Trade, *supra* note 36, at §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) *available at* 2003 WL 21729286.

²⁹⁹ U.S. Drug Enforcement Administration, Drug Trafficking in the United States, Sept. 2001, *available at* <http://www.usdoj.gov/dea/pubs/intel/01020/index.html> (visited July 7, 2004) (2000 data). Retail prices per gram are significantly higher, particularly for smaller quantities.

³⁰⁰ *See supra* note 295.

³⁰¹ OFFICE OF NATIONAL DRUG CONTROL POLICY, TRENDS IN COCAINE PRICES (1981-2000) (price per gram for purchase of 1 to 10 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>.

³⁰² From a hopelessly anecdotal source, a travel journal of an American using drugs in Columbia. David Ashley, Cocaine in Columbia, <http://www.erowid.org/experiences/exp.php?ID=1796> (last visited—the website, not Columbia—July 9, 2004).

³⁰³ The numerator is \$100 per gram and the denominator is \$4 per gram.

³⁰⁴ Alliance Against Counterfeiting & Piracy, Proving the Connection: Links Between Intellectual Property Theft and Organised Crime 7-8 (circa 2002) *available at* www.a-cg.com (visited Oct. 7, 2004).

³⁰⁵ One would expect some significant reported court cases over the past 20 years on illegal imports of Indian and other unlicensed generics if the problem was widespread. Andrew Farlow of Oxford finds little evidence of diversion, Andrew Farlow, Costs of Monopoly Pricing Under Patent Protection, Presentation at Columbia University, Dec. 4, 2003, slide 19.

³⁰⁶ DG Trade, *supra* note 36, at §3.3.

US\$18 million were found to have been diverted from West Africa to the EU.³⁰⁷ GlaxoSmithKline sued several participants in the transactions, including a legal parallel trader in pharmaceuticals, Dowelhurst Ltd, for trademark infringement.³⁰⁸

The Dowelhurst case unearthed several remarkable facts which undercut the public relations spin that Glaxo had put on the case. First, 99% 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.³⁰⁹ 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.³¹⁰ Second, 99% of the packages had been sold within Europe, to addresses in France, and probably never made the trip to Africa.³¹¹ The alleged diversions occurred in Europe, not in Africa. I say alleged diversions, because the case clearly says that the resale of the drugs was not proscribed by contract.³¹² Third, by placing the packages into commerce within Europe, Glaxo exhausted its IP rights within Europe.³¹³ Finally, Glaxo sold the packages without any attempt to label them as ineligible for sale or re-importation into the EU. They were packaged in French, with EMEA license codes and nothing was done to indicate they were destined for a charitable access program.³¹⁴ 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.³¹⁵ Within three weeks of the Glaxo diversion story, the European Commission announced plans to issue a regulation to curb such diversions.³¹⁶ The 2003 Council Regulation promptly required many modifications to packages and pills destined for essential access programs.³¹⁷

³⁰⁷ A sample of media reports from three continents in October 2002 include: Gautam Naik, *Profiteers Divert to Europe AIDS Drugs Meant for Africa*, Asian Wall St. J., Oct. 7, 2002, at A9; Sarah Boseley & Rory Carroll, *Profiteers Resell Africa's Cheap Aids Drugs*, The Guardian, Oct. 4, 2002, at P1; *HIV Drugs For Africa Diverted to Europe; Probe Targets Wholesalers*, Wash. Post, Oct. 3, 2002, at A10. See also Dukes, *supra* note 76, at 50, n.1.

³⁰⁸ *Glaxo Group Ltd v. Dowelhurst Ltd*, [2004] E.T.M.R. 39 (July 31, 2003) available at 2003 WL 21729286.

³⁰⁹ *Id.* at ¶36.

³¹⁰ *Id.* at ¶46. The Deputy Judge imposed over 90% of the litigation costs on Glaxo, in part because he felt misled. *Glaxo Group Limited v. Dowelhurst Limited*, [2003] E.W.H.C. 3060 (High Court, Ch. Div. 2003) available at 2003 WL 23014797, at ¶¶ 10, 17.

³¹¹ *Glaxo Group Ltd v. Dowelhurst Ltd*, [2004] E.T.M.R. 39 (July 31, 2003) available at 2003 WL 21729286, at ¶¶ 66-76. Only 1% of the packages had actually been sold to a buyer in Africa, namely the packages involved in the access program.

³¹² *Id.* at ¶ 39.

³¹³ *Id.* at ¶¶ 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 Limited v. Dowelhurst Limited*, [2004] E.W.C.A. Civ. 290 (Court of Appeal, Civ. Div., 2004) available at 2004 WL 412961. Specifically, the Court of Appeals upheld the exhaustion rule on 100% of the packages rather than just 99%. *Id.* at ¶¶ 30-40.

³¹⁴ *Glaxo Group Ltd v. Dowelhurst Ltd*, [2004] E.T.M.R. 39 (July 31, 2003) available at 2003 WL 21729286, at ¶¶ 46-50.

³¹⁵ *Id.* at ¶¶51-53.

³¹⁶ *EU/WTO – Plan to Curb Illicit Medicines Trade*, Eur. Rep. Oct. 26, 2002 (no page number available) available at 2002 WL 13768322.

³¹⁷ At present, the EU Council Regulation only applies to "tiered price" pharmaceutical exports to 76 listed developing and least-developed countries and to "HIV/AIDS, malaria, tuberculosis and related

The only other major media report of diversion of essential access drugs was in *Forbes* in April 2004, noting diversions in Indonesia, Chile and Lebanon.³¹⁸ 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.³¹⁹ This is a simple case of local corruption, and there is no evidence that the drugs are 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.³²⁰ 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 arbitrage market in ARVs from low income markets 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,³²¹ subject to complex rules on repackaging and trademark infringement devised by the European Commission and the European Court of Justice.³²² In the EU, illegal pharmaceutical arbitrage is rarely observed.³²³

opportunistic diseases," (a limitation which should be amended following Cancun). The EU defines a "tiered price" pharmaceutical as being offered to the poor for either direct manufacturing cost plus no more than 15% or at less than 25% of the OECD weighted average ex-factory price. Council Regulation 953/2003 to avoid trade diversion into the European Union of certain key medicines, art. 7, 2003 O.J. (L135/6) art. 3(a).

³¹⁸ Richard C. Morais, "Pssst ... Wanna Buy Some Augmentin?" *Forbes* 2000, April 12, 2004 available at http://forbes.com/forbes/2004/0412/112_print.html.

³¹⁹ *Id.*

³²⁰ Judd, *supra* note 297.

³²¹ PETER WEST & JAMES MAHON, BENEFITS TO PAYERS AND PATIENTS FROM PARALLEL TRADE (York Health Economics Consortium Working Paper, May 2003) (estimating direct savings of € 631 million in 2002 from legal pharmaceutical arbitrage (parallel trade) within the EU) (funded by a grant from European parallel traders); *but see* KANAVOS ET AL., *supra* note 45, at 15-16 (finding meager benefits to consumers from parallel pharmaceutical trade) (funded by and unrestricted grant from Johnson & Johnson) available at <http://www.lse.ac.uk/collections/LSEHealthAndSocialCare/documents/otherpaperseries.htm>.

³²² For a recent discussion, *see* Boehringer Ingelheim KG v. Swingward Ltd, [2004] E.T.M.R. 65 (Mar. 5, 2004) available at 2004 WL 343819, at ¶¶ 3-17.

³²³ *See supra* Section VI.C.2.a.

Canada provides a contrasting example. Pharmaceutical arbitrage from Canada to the U.S. operated for years under legal ambiguity. Proponents occupied the moral high ground of 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.³²⁴

So the first imperative is to prevent any legal or moral uncertainty concerning dysfunctional arbitrage. At a minimum, diversion to high income country markets of drugs intended for the poor should be clearly illegal. The EU, for example, promptly moved in this direction following media reports of the Glaxo diversion.³²⁵ The US should follow suit.

The second task is to modify the product to resist substitutability. The pharmaceutical manufacturing process could be altered to create multiple versions of any prescription drug, distinguished by radically different colors, shapes, names, sizes and packaging. Markets must be segmented into commercial and charitable markets, and never the twain shall meet. The Cancun General Council Decision addresses this issue: exporting countries must clearly identify the products through labeling or marking and through special coloring or shaping.³²⁶ The EU Council Regulation follows this tact.³²⁷ GlaxoSmithKline and others are complying, altering both the packaging and the color of the product.³²⁸ 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 access medicines to a reputable supply chain located outside of the US or EU, if domestic exhaustion is to be avoided.

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: “those pills may not be safe,” since Africans will be told exactly the opposite: “the red pills are safe and effective.”³²⁹ 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.³³⁰ Under the EU Council Regulation, all covered pharmaceuticals exported from the EU will bear a special logo identifying the product as destined for the

³²⁴ See *infra* Section VII.A.1

³²⁵ See Council Regulation 953/2003 to avoid trade diversion into the European Union of certain key medicines, art. 7, 2003 O.J. (L135/6) art. 3(a).

³²⁶ *Cancun General Council Decision*, *supra* note 139, at ¶ 2(b).

³²⁷ Council Regulation 953/2003 to avoid trade diversion into the European Union of certain key medicines, art. 7, 2003 O.J. (L135/5) ¶10. While the Council Regulation addresses importation in luggage for personal use, similar to the U.S. personal importation rule, it does not address (but probably covers) internet sales. *Id.* at ¶13, art. 10. Seized product may be used for humanitarian purposes. *Id.* at ¶14.

³²⁸ GLAXOSMITHKLINE PLC, 2003 ANNUAL REPORT, Form 20-F, at 29.

³²⁹ Vertical product differentiation based on quality is common in some products (regular v. premium gasoline), but is probably untenable in pharmaceuticals.

³³⁰ If the arbitrated drugs were voluntarily sold rather than stolen, then the moral claim weakens.

poor.³³¹ In addition, domestic law within the high income countries should criminalize the practice.

The final front for anti-diversion measures are the borders of the high income countries. Pharmaceutical arbitrage may become dysfunctional 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.³³² 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. High Income Markets Should 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. All five measures do not 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.³³³ 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.”³³⁴ Under Cancun, developing and least developed countries inappropriately bear these costs even if global patent rents are supra-optimal.³³⁵

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 current distribution system.³³⁶ This is not a best-case result, but certainly is not an enforcement priority. The priority should be on weaknesses in the supply chain where

³³¹ Council Regulation 953/2003 to avoid trade diversion into the European Union of certain key medicines, art. 7, 2003 O.J. (L135/7). The logo is found in Annex V of the regulation.

³³² See *supra* Section V.D.2.

³³³ Barton Gellman, *supra* note 136.

³³⁴ *Cancun General Council Decision*, *supra* note 139, at ¶ 4.

³³⁵ If global patent 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.

³³⁶ This appears to be the case in Jakarta. Richard C. Morais, “Pssst ... Wanna Buy Some Augmentin?” *Forbes* 2000, April 12, 2004 available at http://forbes.com/forbes/2004/0412/112_print.html.

large batches could be diverted in a single transaction. The risk may be greatest while the product is still outside of the recipient country.³³⁷

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 patent rents, but will not harm innovation if patent rents are supra-optimal.

3. Counterfeit Drugs

In the debates over essential medicines, care must be taken to distinguish arbitrage from counterfeiting. For example, a August 10, 2004 article on Internet drug purchases in the Wall Street Journal used the words “fake” or “counterfeit” many times, before mentioning that FDA lab tests “showed that most of the drugs contained too much active ingredient, making the fakes potentially harmful.”³³⁸ These drugs may be poorly produced, or too strong by U.S. standards, but they should not be called counterfeits.³³⁹ In copyright and patent practice, a ‘counterfeit’ or ‘pirated’ copy is one that was manufactured by an unlicensed source, but it might well be as functional as the genuine article.³⁴⁰ In pharmaceuticals, the term ‘counterfeit’ should be reserved for a drug which does not contain the proper active ingredient.³⁴¹ In this Article, a safe and effective pill which comes from an unauthorized manufacturer is denominated an ‘unlicensed’ product.

Empirical evidence suggests that virtually all of the internationally arbitrated drugs arriving in the US are not counterfeits by this definition.³⁴² These drugs might violate restrictions on parallel importation, FDA approval or labeling, or other laws, but they are not counterfeit. Most of the counterfeit drugs in the U.S. have domestic origins

³³⁷ Both conditions were present in the Glaxo case.

³³⁸ Heather Won Tesoriero, *Fake-Drug Sites Keep a Step Ahead*, Wall St. J., Aug. 10, 2004, at D4. See also Mark McClellan, Testimony before the Senate Committee on Commerce, Science & Transportation, March 11, 2004 (discussing “unapproved, imported pharmaceuticals” and “unsafe and illegal drugs” with “ineffective, counterfeit” drugs) (McClellan was at the time the Commissioner of the Food and Drug Administration; he currently heads the Centers for Medicare and Medicaid Services).

³³⁹ The trade association of European pharmaceutical research companies and the WHO use the broader definition. EUROPEAN FEDERATION OF PHARMACEUTICAL INDUSTRIES AND ASSOCIATIONS, INTERNATIONAL EXHAUSTION OF TRADE MARK RIGHTS 5 (April 2001). My point is not to argue who’s definition is ‘right,’ but to demonstrate the analysis which is possible when using a narrower definition.

³⁴⁰ A counterfeit Gucci purse might nevertheless be a fully functional and stylish purse. A counterfeit music CD contains authentic, but unlicensed, recordings. Pharmaceuticals may contain sub-therapeutic doses of the active ingredients; be improperly packaged, labeled, or stored; or may contain improper contaminants. These drugs are substandard rather than being counterfeit.

³⁴¹ The FDA definition is broader, including drugs with improper dosages, sub-potent or super-potent ingredients, or contamination. U.S. Food & Drug Admin., FDA’s Counterfeit Drug Task Force Interim Report 5 (Oct. 2003) available at http://www.fda.gov/oc/initiatives/counterfeit/report/interim_report.html (visited Oct. 1, 2004). This improperly conflates counterfeits with poorly manufactured or stored product.

³⁴² In the FDA seizures of imported drugs, no counterfeit drugs were found, FDA Press Release, 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).

or domestic networks,³⁴³ but the FDA still considers it a relatively rare practice,³⁴⁴ which is nevertheless growing rapidly.³⁴⁵ In 2000, the estimated value of EU pharmaceutical counterfeiting was Euro 1.554 billion. The UK-based Anti-Counterfeiting Group estimated in 2003 that 5.8% of pharmaceutical company annual revenue is lost due to counterfeiting.³⁴⁶ 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.³⁴⁷ 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.³⁴⁸ 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 but 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 arbitrated ARVs might be possible, obtaining them in sufficient quantities would require a procurement team in the field (sub-Saharan Africa), with multiple diversions against an alerted supply chains, followed by repackaging and a reverse supply chain back to high income country markets. Counterfeits could be appropriately labeled and packaged, rather than having pills in the wrong color and packaging labeled for essential medicine programs. These characteristics enable counterfeits to be introduced into high income country supply chains directly, and much easier than diverted pills from Africa. Counterfeiting dispenses with many costs. The per pill cost to produce a placebo without active ingredients may be far cheaper than covert

³⁴³ Mary Pat Flaherty, *US Prescription Drug System Under Attack: Multibillion-Dollar Shadow Market is Growing Stronger*, Wash. Post, Oct. 19, 2003, at A1.

³⁴⁴ FDA, Counterfeit Drug Task Force Interim Report 3 (Oct. 2003).

³⁴⁵ The FDA estimates that pharmaceutical counterfeiting has increased four fold in the past few years. See *The Washington Post* series of articles on counterfeit drugs which ran in Fall 2003 by Mary Pat Flaherty and Gilbert M. Gaul. 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. The Wall Street Journal has also covered the story. Anna Wilde Mathews and Heather Won Tesoriero, *Murky Channels: Bogus Medicines Put Spotlight On World of Drug Distributors*, WALL ST. J., Sept. 29, 2003, at A1.

³⁴⁶ The Anti-Counterfeiting Group, *Why You Should Care About Counterfeiting 14* (circa 2003) available at www.a-cg.com (visited Oct. 7, 2004).

³⁴⁷ Alliance Against Counterfeiting & Piracy, *supra* note 304, 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.”).

³⁴⁸ The business plan of the Cali drug cartel probably includes a quality assurance mechanism. See the interesting (and merely conjectural) marketing plan for the Cali Cartel by Matthew Kwan, completed during his MBA studies at the Melbourne Business School, <http://www.darkside.com/au/mba/cali.html> (visited July 8, 2004).

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.³⁴⁹ A criminal is unlikely to counterfeit a pill and sell it as aspirin or Triomune, when it could be sold as Lipitor or Fuzeon. When low-cost unlicensed 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. 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.³⁵⁰

4. 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.³⁵¹ 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.³⁵² Grant 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

³⁴⁹ The examples of counterfeits in most media and FDA reports are of expensive patented drugs such as Lipitor, Epogen, Zyprexa and Serostim. See Leila Abboud, Anna Wilde Mathews & Heather Won Tesoriero, *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.

³⁵⁰ Some steps towards an anti-counterfeiting policy are being taken by the FDA Task Force. FDA, Counterfeit Drug Task Force Interim Report 18-22 (Oct. 2003) available at http://www.fda.gov/oc/initiatives/counterfeit/report/interim_report.html.

³⁵¹ THE PRESIDENT'S EMERGENCY PLAN FOR AIDS RELIEF: U.S. FIVE-YEAR GLOBAL HIV/AIDS STRATEGY 16 (Feb. 23, 2004).

³⁵² GLOBAL FUND, GUIDE TO THE GLOBAL FUND'S POLICIES ON PROCUREMENT AND SUPPLY MANAGEMENT (April 2004).

local collective preferences. Similar choices may be made between licensed drugs and unlicensed 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 unlicensed generics.³⁵³ PEPFAR requires approval by a "stringent regulatory authority" before procurement, meaning the NDRAs from the U.S., EU and Japan (the ICH), and possibly Canada.³⁵⁴ 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.³⁵⁵ PEPFAR will impose "all FDA standards for drug safety, efficacy, and quality,"³⁵⁶ even though existing studies have proven the efficacy of ARV treatment with unlicensed generics.³⁵⁷ PEPFAR is also creating its own supply chain management system, independent of The Global Fund.³⁵⁸ These efforts are duplicative and will inevitably raise costs and delay treatment.³⁵⁹ Amazingly, the U.S. funds both programs, and remains the largest donor to The Global Fund.³⁶⁰

³⁵³ From the beginning, PEPFAR guidance to its field offices prohibited acquisition of cheaper generic FDCs. GAO, U.S. AIDS COORDINATOR ADDRESSING SOME KEY CHALLENGES TO EXPANDING TREATMENT, BUT OTHERS REMAIN 37 (GAO Report GAO-04-784, July 2004). A cynic might view 'highest quality' as merely a stalking horse for 'highest price.'

³⁵⁴ *Id.* at 19-37.

³⁵⁵ 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>; Gautam Naik, Mark Schoofs & Sarah Lueck, *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 D 5 (raising unresolved questions about whether the Office of the U.S. Global AIDS Coordinator will procure generic AIDS drugs at the lowest possible price).

³⁵⁶ RANDALL L. TOBIAS, U.S. GLOBAL AIDS COORDINATOR, TESTIMONY BEFORE THE U.S. SENATE COMMITTEE ON APPROPRIATIONS, SUBCOMMITTEE ON FOREIGN OPERATIONS, May 18, 2004.

³⁵⁷ 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 (background document for WHO meeting on Fixed Dose Combinations for HIV/AIDS, Tuberculosis, and Malaria) (Nov. 18, 2003); 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 (July 3, 2004); Gregory K. Robbins, et al., *Comparison of Sequential Three-Drug Regimens as Initial Therapy for HIV-1 Infection*, 349 *N. Eng. J. Med.* 2293 (Dec. 11, 2003); and 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 *N. Eng. J. Med.* 2304 (Dec. 11, 2003).

³⁵⁸ U.S. AGENCY FOR INTERNATIONAL DEVELOPMENT, DRAFT STATEMENT OF WORK PUBLISHED FOR COMMENT—SUPPLY CHAIN MANAGEMENT SYSTEM FOR THE PRESIDENT'S EMERGENCY PLAN FOR AIDS RELIEF (June 7, 2004).

³⁵⁹ *See, e.g.*, GAO, *supra* note 353; Mark Schoofs, *At Zimbabwe Clinic, Wait Is Long And U.S. Drug Cupboard Is Bare*, WALL ST. J., July 1, 2004, at A8.

³⁶⁰ GLOBAL FUND FOR AIDS, TB & MALARIA, ANNUAL REPORT 2003.

Three aspects of PEPFAR are worthy of detailed discussion. PEPFAR erects hurdles to procurement of unlicensed generic ARVs in order to steer additional volume at higher prices to PhRMA companies. It establishes a separate supply chain, permitting the U.S. to maximize protection against diversion and arbitrage.³⁶¹ And, finally, it controls quality and delays the onset of resistance. My recommendations to PEPFAR's administrators are as follows:

a. Purchase Unlicensed 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 55% of the U.S. appropriations to be used in treatment, and 75% of that amount (or 41.25% of the total) to be spent on ARVs for fiscal years 2006 through 2008.³⁶² Blocking generic ARVs will funnel \$6.18 billion dollars in additional ARV sales to PhRMA companies,³⁶³ at a price much higher than generics.³⁶⁴ 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 efforts to minimize drug diversion within the recipient countries.³⁶⁵ These costs should be balanced against the benefits of averted arbitrage. As demonstrated in Section V.D.2 above, most arbitrage is not harmful to innovation, and modest levels of dysfunctional arbitrage may be tolerable, particularly in conditions of supra-optimality.

c. Unlicensed Generic FDCs Delay Resistance

³⁶¹ U.S. AGENCY FOR INTERNATIONAL DEVELOPMENT, *supra* note 358, at 6.

³⁶² United States Leadership Against HIV/AIDS, Tuberculosis, and Malaria Act of 2003, Pub. L. No. 108-25, §403 (2003).

³⁶³ 41.25% of \$15 billion.

³⁶⁴ GAO, *supra* note 353, 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).

³⁶⁵ GAO, *supra* note 353, at 44.

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 unlicensed 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-dose Artesunate Combination Therapy or FACT), the most effective treatment for managing malarial resistance will be unnecessarily delayed,³⁶⁶ despite the fact that WHO has already prequalified a FACT.³⁶⁷

VII. 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 'Boston Tea Party of the 21st Century.'³⁶⁸ 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 is unlikely to harm innovation, absent transparent access to PhRMA company data to prove the contrary.

A. The Opportunity for Arbitrage

Patented drug prices in the United States are generally the highest in the world.³⁶⁹ Most other OECD countries have regulatory structures which significantly limit prices

³⁶⁶ For a description of the effort to create FDCs for malaria in Africa and Latin America, see Press Release, DNDi, Malaria Patients Enter DNDi Clinical Trials (July 2, 2004); 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).

³⁶⁷ WORLD HEALTH ORG., ACCESS TO ARTEMISININ-BASED COMBINATION ANTIMALARIAL DRUGS OF ACCEPTABLE QUALITY (2d Ed. April 26, 2004), available at <http://mednet3.who.int/prequal/> (visited July 19, 2004) (Artemether/Lumefantrine FDC manufactured by Novartis).

³⁶⁸ Senator Joe Lieberman, Democratic Presidential Debate in Goffstown, New Hampshire, Jan. 22, 2004, available at <http://www.washingtonpost.com/wp-dyn/articles/A39875-2004Jan22.html>, quoted in Donald L. Bartlett & James B. Steele, *Why We Pay So Much for Drugs*, TIME, Feb. 2, 2004, at 46,

³⁶⁹ U.S. patented prescription drug prices are the highest of any major market, with the possible exception of Japan. Danzon & Furukawa, *supra* note 162, at exh. 3. Generic drugs, unprotected by patents or

for patented pharmaceuticals.³⁷⁰ Canada's Patented Medicine Prices Review Board³⁷¹ helps to keep Canadian prices significantly lower than U.S. prices for patented drugs.³⁷² 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 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

exclusive marketing periods, are generally priced competitively in the U.S. Comparisons of international drug prices should not conflate the categories. Danzon and Furukawa fault other studies for excluding generics since they represent significant volumes in the OECD. *Id.*, at 4. However, generics must be excluded when calculating patent rents or the potential for arbitrage in patented drugs. Canadian prices are 64% of U.S. prices for patented drugs, and somewhat higher for generics, yielding a net differential of 6%. *Id.* at ex. 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] (generics generally cheaper in the U.S. compared to Canada). Thus the potential for arbitrage lies in the 36% differential in patented medications, not the 6% overall figure.

³⁷⁰ ROTHNIE, *supra* note 57, at 491 ffg. (general, but dated, discussion of EU pharmaceutical price controls); *see also* Danzon et al., *supra* note 174 (pharmaceutical companies delay launch of new drugs in EU countries with strict price controls to reduce risk of parallel trade).

³⁷¹ Since 1988, Canada regulates patented drug prices through the Patented Medicine Prices Review Board, a quasi-judicial board with can bring proceedings against PhRMA companies which charge excessively high prices. Maria Barrados, et al., 1998 Report of the Auditor General of Canada, ¶17.93 (Sept. 1999) available at <http://www.oag-bvg.gc.ca>; Dr. Robert G. Elgie, Canada's Patented Medicine Prices Review Board: New Approaches (Drug Industry Ass'n Washington Conference on Pharmaceutical Pricing and Reimbursement: What New Variables are at Work? 3-4 (Patented Medicine Prices Review Board, Ap. 16, 1999), <http://www.pmprb-cepmb.gc.ca>. The Board has constrained some patented drug prices in Canada. Barrados, *supra*, at ¶17.25. Since the creation of the Board, patented pharmaceutical prices in Canada have increased only 1% per year on average. Elgie, *supra*, at 6. Nevertheless, Canada's system is not strictly a price control or rate setting system, but a soft reference price system with a quasi-judicial process. Barrados, *supra*, at ¶17.50 – 17.56; Elgie, *supra*, at 6.

³⁷² Many surveys have documented the price differential between U.S. and Canadian patented pharmaceuticals. *See, e.g.*, Ram Kamath & Scott McKibbin, Office of Special Advocate for Prescription Drugs, State of Illinois, Report on Feasibility of Employees and Retirees Safely and Effectively Purchasing Prescription Drugs from Canadian Pharmacies 79 (2003) (39% savings on the drugs that Illinois purchases that could be safely imported from Canada); Danzon & Furukawa, *supra* note 162, at ex. 4 (patented drugs are 36% cheaper in Canada compared with U.S.); *Savings Immense on Canadian Drugs*, WASH. TIMES, Nov. 5, 2003, at [SC: Pincite needed] (33% to 80% cheaper for the 10 most popular drugs).

Canada. Consumer arbitrage began to erode differential pricing between U.S. and Canadian drug prices.

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

1. The Internet Enables More Extensive Arbitrage

The Internet dramatically altered the potential for pharmaceutical arbitrage. The transaction cost of importing a prescription from Canada dropped to a small fraction of the arbitrage savings.³⁷³ Many Canadian websites began to compete for the American consumer's attention. These factors multiplied the possible arbitrage market. The potential number of buyers for cross-border arbitrage jumped from several million Americans living near the Canadian border to the entire wired population of the United States. In last several years, the potential number of buyers expanded again, as U.S.-based companies began to facilitate internet ordering of pharmaceuticals for unwired consumers, particularly the elderly. Health insurers and some government officials began to encourage consumers to acquire cheaper medicines from Canada. The media devoted increasing attention to the phenomenon from 1999, raising awareness amongst consumers that arbitrage was an option. A large and growing portion of the most valuable market for patented pharmaceutical medications is now only a click away from arbitrage.

If this process continues unchallenged, one would expect institutions such as hospitals, nursing homes, and retail pharmacies to begin to source from Canada. Payors such as health plans³⁷⁴ and governments³⁷⁵ 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,³⁷⁶ with potential savings of \$90.7 million per year.³⁷⁷

³⁷³ For a patient with annual out of pocket prescription costs of \$2000, a reasonable amount of search costs can be justified to save 30%.

³⁷⁴ United States-based PBMs are paying claims today from Canadian pharmacies, supporting the patient's decision to import, Kamath & McKibbin, *supra* note 372, 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, and States such as West Virginia.

³⁷⁵ 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 372, at 3, 30.

³⁷⁶ Kamath & McKibbin, *supra* note 372, at 79-81.

³⁷⁷ Kamath & McKibbin, *supra* note 372, at 19 (cost savings assumes all employees and retirees will participate).

Several other states are exploring similar programs.³⁷⁸ 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.³⁷⁹ In October 2003, an FDA official estimated that 3 million U.S. prescriptions per year were being filled from Canada,³⁸⁰ yielding an estimated arbitrage market size of \$600 to 700 million per year in 2003.³⁸¹ IMS estimates US\$1.1 billion (in U.S. prices) in 2003, an increase of 70% over 2002.³⁸² 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,³⁸³ 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;³⁸⁴ normal U.S. prices will not fall unless the PhRMA companies agree to reduce their

³⁷⁸ See, e.g., Katherine M. Skiba, *Doyle Makes Case for Buying Cheaper Drugs from Canada*, MILWAUKEE SENTINEL-JOURNAL, Feb. 24, 2004; Fred Frommer, *Pawlenty Tries to Win FDA over on Drug Plan*, MINNEAPOLIS STAR TRIBUNE, Jan. 16, 2004 (Minnesota Governor's attempt to win FDA approval for drug importation plan); Tony Leys, *Vilsack Offers Plan on Canadian Drugs*, DES MOINES REGISTER, Jan. 22, 2004 (Iowa's plan).

³⁷⁹ Heffler, *supra* note 104, at exh. 1. This number includes only retail sales of prescription drugs, excluding purchases of prescription drugs by institutions such as hospitals and nursing homes. The all-inclusive number for 2004 is closer to \$250 billion. SAGER & SOCOLAR, *supra* note 11, at 4, n. 25.

³⁸⁰ Transcript of motion for preliminary injunction at 127-28, *United States v. Rx Depot, Inc.*, No. 03-CV-0616-EA (M) (N.D. Ok. Oct. 8-9, 2003) (examination of Thomas McGinnis, Director of Pharmacy Affairs, FDA) (on file with author) [hereinafter Rx Depot Transcript].

³⁸¹ While the average size of U.S. – Canadian prescriptions are unknown, data from the State of Illinois describes consumer co-pays of at least \$40 per prescription, Kamath & McKibbin, *supra* note 372, at 5, implying a retail price of \$200 at a 20% co-pay. One internet facilitator's data indicated an average Canadian prescription price of \$220. Private interview by author, October 2003. Recent Canadian estimates suggest a market of \$700 to \$800 million per year. Tamsin Carlisle, *Some Online Pharmacies Aren't Filling Big Orders Due to Fears of Shortages*, WALL ST. J., Dec. 26, 2003, at A9; Tony Pugh, *Low-Cost Drug Sales to U.S. Should Stop, Canadian Group Says*, PHILADELPHIA INQUIRER, Nov. 16, 2003, [SC: **pincite needed**]. 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 USA. PHARMA MARKETLETTER (May 17, 2004). By comparison, the domestic U.S. prescription mail order market was \$20.7 billion in 2001. NIHCM, *supra* note 54, at 9.

³⁸² Paul Saatsoglou of IMS Health *quoted in* Richard C. Morais, "Pssst ... Wanna Buy Some Augmentin?" *Forbes* 2000, April 12, 2004 available at http://forbes.com/forbes/2004/0412/112_print.html.

³⁸³ Canadian Institute for Health Information, *supra* note 71, 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).

³⁸⁴ 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. 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.

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.³⁸⁵ With negligible transaction and information costs, a fungible 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.³⁸⁶

Canadian arbitrage may destroy the differential pricing system which kept U.S. drug prices the highest in the world. Erosion of differential pricing will shift consumer surplus from producers to consumers. American consumers will save many billions of dollars on pharmaceuticals, greatly improving financial access. The other side of the coin is that PhRMA companies may lose the lion's share of their worldwide profits.³⁸⁷ One unasked question is whether this process will result in sub-optimal patent rents. Supporters of pharmaceutical companies simply assume that drug innovation will be hindered. So long as patent rents remain supra-optimal, Canadian arbitrage improves consumer welfare without harming innovation.

2. Regulatory Arbitrage

A process similar to arbitrage also occurs between regulatory systems. Within the United States, if one particular state imposes draconian regulations upon businesses, the business owners may vote with their feet by relocating to a more attractive regulatory environment. If sufficiently important firms relocate, or credibly threaten to do so, then the state may reconsider its stance and ameliorate the harsh regulations.³⁸⁸

A variation of this process is at work in Canadian arbitrage. In the United States, pharmaceutical companies have been largely successful in blocking the adoption of price controls for its products.³⁸⁹ Other nations, such as Canada, have imposed more restrictive

³⁸⁵ 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 45, at 136 (disproving the price convergence hypothesis).

³⁸⁶ A recent CBO issue brief suggests that the net effect on U.S. prices from Canadian arbitrage will be small. CBO, WOULD PRESCRIPTION DRUG IMPORTATION REDUCE U.S. DRUG SPENDING? (Apr. 29, 2004). The CBO assumed that arbitrage supplies would be successfully interdicted by PhRMA companies, capping the arbitrage at 10 to 15% of the 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 10 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 10 years.

³⁸⁷ 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' profit.) The question will turn on whether pharmaceutical demand is relatively inelastic. *Id.* at 11-13.

³⁸⁸ The classic work is Charles Tiebout, *A Pure Theory of Local Expenditures*, 64 J. POL. ECON. 416 (1956).

³⁸⁹ The industry strongly oppose price controls. Sidney Taurel, *Hands Off My Industry*, WALL ST. J., Nov. 3, 2003, at A14 (Taurel is President, Chairman and CEO of Eli Lilly).

regulatory measures to reduce patent rents.³⁹⁰ One perspective on this cross-border arbitrage is that some Americans have imported Canada's pricing regulatory system into the U.S. for outpatient non-emergency pharmaceuticals.³⁹¹ Regulatory arbitrage is at work between the U.S. 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.³⁹² The certification proved to be the Achilles heel, since HHS has refused to issue the certification.³⁹³ 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.³⁹⁴ The Pharmaceutical Market Access Act of 2003, also passed by the House, permitted imports from 25 countries with effective NDRA's.³⁹⁵ The Senate version of the bill reinstated the certification requirement, effectively gutting Canadian importation under the Bush Administration.³⁹⁶ 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.³⁹⁷

³⁹⁰ Many discussions of Canada's patented pharmaceutical pricing system wrongly assume it includes mandatory price controls. Canada's Patented Medication Prices Review Board uses a soft reference prices and quasi-judicial processes to regulate the ex-factory prices within Canada. The Board also encourages R&D at a minimum level of 10% of revenues, and grants special pricing consideration to breakthrough drugs. Barrados, *supra* note 371, at ch. 17; Elgie, *supra* note 371, at 3-4. Thus, Canada's system is one attempt to optimize patent rents, striking a balance between cost, quality and access, based upon imperfect data.

³⁹¹ The American Enterprise Institute identifies this as a major weakness of proposals to permit re-importation from Canada. JOHN E. CALFEE, *THE HIGH PRICE OF CHEAP DRUGS*, (Jul. 14, 2003), <http://www.aei.org> [SC: Use precise URL].

³⁹² Medicine Equity and Drug Safety Act of 2000, Pub. L. 106-387, 114 Stat. 1549A-35.

³⁹³ Sarah Lueck, *Senate Supports Wider Importing of Canada Drugs*, WALL ST. J., June 23, 2003, at A10.

³⁹⁴ Medicare Prescription Drug and Modernization Act of 2003, H.R. 1, 108th Cong. § 1121 (2003) (passed in the House on June 27, 2003). Another bill in the 108th Congress would have permitted re-importation from the EU as well. Save Our Seniors Act of 2003, H.R. 2769, 108th Cong. § 2 (2003).

³⁹⁵ Pharmaceutical Market Access Act of 2003, H.R. 2427, 108th Cong. (2003).

³⁹⁶ Medicare Prescription Drug Improvement and Modernization Act of 2003, 21 U.S.C. § 804 (2004); 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.

³⁹⁷ Henry J. Aaron, *Should Public Policy Seek to Control the Growth of Health Care Expenditures?*, W3 HEALTH AFF. 28- 31 (Web Exclusive, Jan. 8, 2003) [AE/SC: Check how we have cited web exclusives in the past] ("The chances that we will adopt the Canadian or French health care system as a whole are about as good as those that we will join the British Commonwealth or adopt French as a second national language. Even adopting elements of foreign systems is problematic because important aspects of health care financing and delivery are mutually interrelated."). John Calfee of the American Enterprise Institute makes the point that reimportation of pharmaceuticals from Canada is equivalent to importing Canadian price controls. Calfee, *supra* note 391.

Another example of regulatory arbitrage involves the efforts of U.S. psychiatrists to obtain prescribing authority, currently denied to them under U.S. law. Some U.S. psychiatrists direct their patients to Canadian pharmacies, which accept prescriptions written by U.S. psychologists.³⁹⁸ This practice will provide empirical evidence of the medical efficacy of prescriptions by U.S. psychiatrists, 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.³⁹⁹

3. Virtual Arbitrage

The closely-related concept of virtual arbitrage involves foregoing the actual importation of drugs, but using lower observed prices as an external reference price, whether by government regulation or in contract. The U.S. employs a virtual arbitrage system in requiring certain discounts for drugs purchased under Medicaid, discounts which reference other 'best' prices.⁴⁰⁰ West Virginia recently established a State agency which adopted the Federal Supply Schedule as a soft reference price for drug purchases by the State.⁴⁰¹ 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.⁴⁰² 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

³⁹⁸ Linda Temple, *Who Gets to Prescribe? Psychologists Send Drug Orders to Canada, Spark a Medical Debate*, USA TODAY, Dec. 18, 2003, at 10D.

³⁹⁹ Alvarez and Trachtman note that regulatory arbitrage may or may not have positive effects, depending upon the condition of spillovers (negative externalities). Jose E. Alvarez & Joel P. Trachtman, *Institutional Linkage: Transcending "Trade and ..."*, 96 AM. J. INT'L L. 77, 84 (2002) citing Joel P. Trachtman, *Regulatory Competition and Regulatory Jurisdiction*, 3 J. INT'L ECON. L. 331 (2000). In the present case, pharmaceutical regulatory arbitrage is a response to the existing free rider problem of national drug price regulation. This response may well 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 Alvarez and Trachtman's article. Alan O. Sykes remarks that subjecting domestic regulatory systems to the pressures of global trade "need not be unfortunate. International regulatory competition may well drive out foolish and wasteful regulations rather than undermine valuable regulations." ALAN O. SYKES, INTERNATIONAL TRADE AND HUMAN RIGHTS: AN ECONOMIC PERSPECTIVE 17 (Univ. of Chicago John M. Olin Law & Economics Working Paper No. 188, 2d Series, May 2003).

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

⁴⁰¹ WEST VIRGINIA REPORT, *supra* note 164, at 1-7.

⁴⁰² On the issue of the transaction costs of physical arbitrage, *see* the comments by Harvey E. Bale, Jr., the Director-General of the International Federation of Pharmaceutical Manufacturers Associations, in Harvey E. Bale, Jr., *The Conflicts Between Parallel Trade and Product Access and Innovation: The Case of Pharmaceuticals*, 1 J. INT'L ECONOMIC L. 637 (1998). These claims are hotly disputed by proponents of parallel trade in pharmaceuticals. *See, e.g.,* West & Mahon, *supra* note 321.

markets into high income markets must be blocked if differential pricing is to be supported for essential medicines.⁴⁰³

Without clear data on patent rent optimality, no conclusion can be reached as to whether other forms of virtual arbitrage harm innovation. All arbitrage, whether virtual or not, will reduce the surplus captured by the patent holder and shift surplus to the consumer and the arbitrageur; however it begs the question to assume that arbitrage will reduce patent rents to a sub-optimal level. One should not assume that the externality is negative. It is possible that West Virginia's use of an external reference price retains supra-optimal innovation incentives while dramatically lowering the State's costs and improving access.

B. 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.

1. Reducing Arbitrage Demand

a. Legal Interdiction

If transaction costs are raised significantly, at some point the arbitrage transaction will become unrewarding and the market pressure on differential pricing will abate. For consumers, the transactions must be low-risk, particularly with regard to: the legality of the transaction, eligibility for reimbursement from third parties, and the counterparty risk of fraud.⁴⁰⁴

In the first two phases of Canadian arbitrage,⁴⁰⁵ 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.⁴⁰⁶

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,⁴⁰⁷ but

⁴⁰³ See *supra* Section V.D.2.

⁴⁰⁴ 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.

⁴⁰⁵ See *supra* Section VII.A.1.

⁴⁰⁶ The FDA's Personal Use Import Policy may be found at <http://www.fda.gov/ora/import/pipinfo.htm>.

⁴⁰⁷ See, e.g., *United States v. Ramsey*, 431 U.S. 606 (1977) (customs officials permitted to intercept mail for contraband).

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.

Beginning in 2003, the enforcement environment changed.⁴⁰⁸ 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.⁴⁰⁹ The Customs Department has posted clarifications of the personal use exception to discourage importation.⁴¹⁰ 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.⁴¹¹ The FDA has sued facilitators such as Rx Depot for assisting in the importation of prescription drugs.⁴¹² The FDA and state pharmacy investigators have also purchased prescription drugs in undercover operations.⁴¹³ 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 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.

⁴⁰⁸ Thomas M. Burton, *The FDA Begins Cracking Down on Cheaper Drugs from Canada*, WALL ST. J., Mar. 12, 2003, at A1.

⁴⁰⁹ Gardiner Harris and Monica Davey, *F.D.A. Begins Push to End Drug Imports*, N.Y. TIMES, Jan. 24, 2004; 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); *Recent FDA/U.S. Customs Import Blitz Exams Continue to Reveal Potentially Dangerous Illegally Imported Drug Shipments*, FDA NEWS, Jan. 27, 2004.

⁴¹⁰ U.S. Customs and Border Protection, Medication/Drugs, http://www.cbp.gov/xp/cgov/travel/alerts/medication_drugs.xml (visited Feb. 15, 2004).

⁴¹¹ The West Virginia Circuit Court issued a preliminary injunction forbidding enforcement by the West Virginia State Board of Pharmacy against Discount Prescription Center, concluding that Discount Prescription Center was not a pharmacy and did not violate state law. Carole Becker, d/b/a Discount Prescription Center v. West Virginia Board of Pharmacy, No. 03-C-1237, slip op. at 11-12 (Cir. Ct. Kanawha Co. Nov. 3, 2003).

⁴¹² Rx Depot was shut down by a preliminary injunction granted by District Court Judge Claire V. Eagan on November 6, 2003. United States v. Rx Depot, Inc., No. 03-CV-0616-EA (M), slip op. at 2-4 (N.D. Ok. Nov. 6, 2003).

⁴¹³ Rx Depot Transcript, *supra* note 380, at 16-40.

Raising information costs may also support product differentiation and discourage substitution.⁴¹⁴ 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.⁴¹⁵ These consumers are relying on the effectiveness of the Health Canada's Therapeutic Product Directorate (TPD), assuming that Canadian drugs are generally as safe as U.S. drugs regulated by the FDA. If the safety or equivalence of drugs from Canadian internet pharmacies are in doubt, this assumption dissolves and risk averse consumers are less likely to arbitrage. Supporters of importation take the opposite tact. In October, 2003, the State of Illinois released a major report in support of importing patented drugs from Canada. The report concluded that the Canadian drug supply was actually more secure than the U.S.⁴¹⁶

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.⁴¹⁷ Questions have been raised as to whether the drugs are produced and transported under FDA standards of safety.⁴¹⁸ Labeling issues, such as the Canadian label for Accutane, have been identified.⁴¹⁹ The actual source of arbitrated 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.⁴²⁰

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.⁴²¹ 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 U.S.

⁴¹⁴ Philips, *supra* note 37, at ch. 12.

⁴¹⁵ Raising search costs for these consumers should hinder arbitrage and support differential pricing. *See* Philips, *supra* note 37, at ch. 12. **[SC: Please provide page numbers rather than chapter reference][ED: the entire chapter is relevant]**

⁴¹⁶ Kamath & McKibbin, *supra* note 372, 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).

⁴¹⁷ *See, e.g.*, FDA NEWS, RECENT FDA/U.S. CUSTOMS IMPORT BLITZ EXAMS CONTINUE TO REVEAL POTENTIALLY DANGEROUS ILLEGALLY IMPORTED DRUG SHIPMENTS (Jan. 27, 2004).

⁴¹⁸ Rx Depot Transcript, *supra* note 380, at 16-158.

⁴¹⁹ *Id.* at 77, ln. 22 (cross-examination of Melvin Frank Szymanski, consumer safety officer, FDA); Discount Prescription Center

⁴²⁰ Hubbard Letter, *supra* note 369 (noting one instance of a Canadian website shipping an Indian drug); *Savings Immense on Canadian Drugs*, WASH. POST, Nov. 5, 2003 ("It is not an answer to this problem to say go buy drugs from Canada, which may be coming from Pakistan and India and China and all those countries we have health concerns about") (Sen. John B. Breaux, D-La).

⁴²¹ Daniel Yee, *CDC: Seniors Prescribed Dangerous Drugs*, Las Vegas Sun, Feb. 9, 2004; 'Lipitor' Surfaces in Counterfeit Probe, WALL ST. J., Dec. 8, 2003, at B8.

c. The Special Case of Re-importation

Questions about production safety, equivalence, and labeling are reduced for a segment of this market known as re-importation. As a matter of production efficiency, pharmaceutical companies do not build plants in every country of the world. Many are located in the United States, including Puerto Rico, where the U.S. government has long encouraged pharmaceutical research and production through generous tax incentives under Section 936 of the Internal Revenue Code.⁴²² 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 U.S., the process is called re-importation.

Concerns about production safety, equivalence, and labeling of re-imported drugs should be carefully scrutinized. The Canadian government is fully satisfied that these drugs are safe, efficacious and properly labeled for Canadian use. The FDA worries about errors in shipping and handling from Canada to the consumer,⁴²³ but these questions are relevant to all mail order pharmaceuticals and are not endogenous to pharmaceutical arbitrage from Canada. The FDA correctly notes that some Canadian standards differ from FDA rules, and forbids re-importation solely on that basis.⁴²⁴ But the missing element is any showing 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.⁴²⁵

The most thorough recent analysis of this question concludes that the Canadian drug supply is actually safer on balance than the U.S. 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.⁴²⁶ The EU has many years of experience with parallel trade in pharmaceuticals, without significant safety issues.⁴²⁷

2. 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.⁴²⁸ Conversely, if supply and demand are unlimited, differential

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

⁴²³ Rx Depot Transcript, *supra* note 380, at 29-31.

⁴²⁴ *Id.* at 28, 76-77.

⁴²⁵ *Id.* at 138-141. *But see* Hubbard Letter, *supra* note 369 (claiming that internet sales from Canada will be more open to counterfeiting).

⁴²⁶ Kamath & McKibbin, *supra* note 372, at 1-5.

⁴²⁷ West & Mahon, *supra* note 321.

⁴²⁸ Janice Haigh, *Parallel Trade: What Next?*, 9 *Pharma Pricing & Reimbursement* 295, 297-98 (October 2004).

pricing will disappear, and a new equilibrium price will prevail in both markets, shifting surplus from the producer to the consumer.

a. Targeting Canadian Internet Pharmacies

Pharmaceutical companies have identified Canadian pharmacies which sell to the U.S. market. These pharmacies have been threatened with a refusal to deal unless the cross-border sales cease.⁴²⁹ This threat not only cuts off the supply for the patented drugs being arbitrated, but it also uses the entire product line as a weapon to enforce differential pricing.

This strategy may not wholly prevent arbitrage. Some doubt the effectiveness or legality of attempts to restrict supply to Canada.⁴³⁰ Members of Congress have asked the U.S. Attorney General to investigate whether antitrust laws are being violated,⁴³¹ and traditional Canadian pharmacies are complaining about the impact of drug company restrictions on their domestic operations.⁴³²

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 U.S. 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.⁴³³ If the concern is truly for patient safety, supply restrictions are a crude and counterproductive tool.

⁴²⁹ Tamsin Carlisle, *Some Online Pharmacies Aren't Filling Big Orders Due to Fears of Shortages*, WALL ST. J., Dec. 26, 2003, at A9; Tony Pugh, *Low-Cost Drug Sales to U.S. Should Stop, Canadian Group Says*, PHILADELPHIA INQUIRER, Nov. 16, 2003, [SC: add pincite]; John O'Connor, *Canadians Warn of Rx Shortage*, CHI. SUN-TIMES, Nov. 13, 2003, [SC: add pincite]; Simon, *supra* note 275; Tamsin Carlisle, *Pfizer Pressures Canadian Sellers of Drugs to U.S.*, WALL ST. J., Jan. 14, 2004, at A6. Similar restrictions have been employed for many years to hinder parallel trade in Europe, Maskus & Ganslandt, *supra* note 46, at 69-70, with limited effectiveness. West & Mahon, *supra* note 321. For the effects of the same tactic on a national level, see Danzon, et al., *supra* note 174.

⁴³⁰ Kamath & McKibbin, *supra* note 372, 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 limiting supply to Canadians 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.”) [SC: Is the w in “we” capitalized in the original?][no]

⁴³¹ Gardiner Harris, *Some in Congress Seek Inquiry Over Drug Supply to Canada*, N.Y. TIMES, Nov. 1, 2003.

⁴³² Carlisle, *supra* note 429; Pugh, *supra* note 429, O'Connor, *supra* note 429.

⁴³³ Kamath & McKibbin, *supra* note 372, 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).

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

Pharmaceutical companies also restrict demand in the U.S. The current market is mostly non-emergency outpatient drugs. For the Medicare population, these drugs have not been covered. If Medicare provided an outpatient drug benefit, a large part of the consumer arbitrage demand would disappear. In 2003, PhRMA reversed its historic opposition to a Medicare drug benefit, and embraced a market-based third party reimbursement plan in Medicare for outpatient drugs.⁴³⁴ The new Medicare drug benefit will reduce consumer demand for arbitrage in an important population and thus support differential pricing.

C. 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. With government support or neutrality, arbitrage would reduce U.S. drug prices as differential pricing between high income markets dissolved. Erosion of differential pricing would lower costs and improve financial access to important drugs.

PhRMA companies bemoan this approach as destructive of long-term research incentives. This is an overly simplistic assessment, for it assumes that patent rents would be sub-optimal at undifferentiated high income market prices. If in fact, Canadian prices are supra-optimal, then Canada is not free riding on American R&D.⁴³⁵ Optimal patent rents would be achieved at prices between current U.S. and Canadian prices. PhRMA companies will be able to compensate for reduced unit prices by increasing volume.

If Canadian prices currently result in supra-optimal patent rents, then extending Canadian prices to the U.S. 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.⁴³⁶ If optimality lies somewhere

⁴³⁴ Prescription Drug and Medicare Improvement Act of 2003, 42 U.S.C. 1395 et seq. [§§ 1860D-1860D-26 of SSA] (2004). This plan also sows the seeds of future government price controls. Once the federal government becomes the payor, price increases are directly translated into budget issues. Medicare providers such as physicians and hospitals were once paid on a fee for service market basis; after years of budgetary issues, Medicare now imposes price controls and rate setting for physician and hospital services. Pharmaceuticals may well follow the same trend line.

⁴³⁵ See Kevin Outterson, *Free Trade Against Free Riders*, 9 *Pharma Pricing & Reimbursement* 254-255 (Sept. 2004).

⁴³⁶ Barrados et al., *supra* note 371, at ¶ 17.11 (Canadian drug companies agreed to increase R&D to 10% of sales by the end of 1996). For current data on Canadian pharmaceutical R&D, see <http://www.canadapharma.org> (the official trade association website).

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 expenditure per capita is up at 10.2% annual growth rates.⁴³⁷ Companies increase their profits in declining unit price markets by increasing unit sales,⁴³⁸ and developing new drugs.⁴³⁹ 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 patent rents were globally sub-optimal. For perhaps the first time, these decisions could be made on the basis of actual data, rather than imprecise estimates.

VIII. Conclusions

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.”⁴⁴⁰ 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 which can be provided on nonrival terms, but are withheld from the poor because of fears of inadequate appropriation.

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.

⁴³⁷ Canadian Institute for Health Information, *supra* note 71, at fig. 19 (stable to declining Patented Medicine Price Index since the introduction of the Patented Medicine Prices Review Board).

⁴³⁸ *Id.* at fig. 13 (annual growth rate of per capita prescribed drug expenditures of 10.2% 1997-2000).

⁴³⁹ *Id.* at 33-43.

⁴⁴⁰ Robin Wright, *A CEO to Direct the AIDS Battle: Former Eli Lilly Chief Comes Out of Retirement*, WASH, POST, Feb. 13, 2004, at A25.