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Improving the Pharmaceutical Industry: Optimality Inside the Framework of the Current Legal System Provides Access to Medicines for HIV/AIDS Patients in Sub-Saharan Africa

Gourav N. Mukherjee

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Improving the Pharmaceutical Industry: Optimality Inside the Framework of the Current Legal System Provides Access to Medicines for HIV/AIDS Patients in Sub-Saharan Africa

Cover Page Footnote

The Author is a J.D. recipient from Florida State University College of Law December 2007. The Author would like to acknowledge the unconditional and loving support of his parents as well as the oversight of Professor Frederick Abbott.

**IMPROVING THE PHARMACEUTICAL INDUSTRY:
OPTIMALITY INSIDE THE FRAMEWORK OF THE
CURRENT LEGAL SYSTEM PROVIDES ACCESS TO
MEDICINES FOR HIV/AIDS PATIENTS IN SUB-SAHARAN
AFRICA**

GOURAV N. MUKHERJEE*

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I. INTRODUCTION

Application of the theories contained in this paper could effect a substantial change on the HIV/AIDS epidemic in Africa through an increase in the availability of essential life saving medicines and a reduction in cost; optimizing within the existing legal framework for our current healthcare system can provide in-

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creased benefits for industry players as well as those in need of medicines.

The author intends to examine and establish a representative model framework under which the current pharmaceutical industry operates. In specific, the framework consists of specific legal and industrial constraints that determine how the participants operate there-in. National Institutes of Health (NIH), universities, other sovereigns or countries, and the pharmaceutical firms participating within the confines of this framework each operate toward certain fundamental objectives that both drive and limit their manner and mode of participation. Pharmaceutical companies aim to achieve, primarily, market or financially driven goals while universities and NIH strive to achieve research efficacy and eventual implementation of effective outcomes in society. Similarly, sovereigns such as Least Developed Countries (LDCs), aim to attain treatment, care, and pharmaceutical products for the members of their populations who inevitably lack the resources to purchase much-needed essential medicines.

The framework consists of constraints, both monetary and non-financial, which steer and confine the participants in the industry. These constraints include government intellectual property rights protection, research funding and efficacy standards, and the ability of certain participants to forgo or exempt themselves from these constraints through compulsory licensing and exemptions to the Agreement of Trade-Related Aspects of Intellectual Property (TRIPS).

Throughout the overall pharmaceutical product realm, this paper will examine the societal objectives for access to medicines, improved research and development efficacy and efficiency, lower cost of finished goods, and improved safety. Through the application of revenue and supply chain optimization techniques, the author intends to demonstrate how the industry can be optimized within the existing legal and social framework and still achieve more of the objectives sought by the participants.

II. CONSTRAINTS IN THE EXISTING FRAMEWORK

Over twenty-two million people have died to date worldwide as a result of HIV/AIDS, and 74% of the forty-two million living people currently infected reside in sub-Saharan Africa.¹ According to the WHO Regional committee for Africa and UNAIDS, it can cost

1. Until There's a Cure: Vital Statistics, <http://www.until.org/statistics.shtml> (last visited Sept. 30, 2007).

between \$130 and \$300 for a one year supply of antiretroviral drugs to treat a patient.²

The existing framework of the current legal system regarding pharmaceutical intellectual property rights will serve as the constraints within which the current system can be optimized. It is not necessary to change or evaluate the potential for changes to the legal system when the current system of constraints and the operation of the governments and pharmaceutical firms is not optimized. As our uppermost constraint, intellectual property rights protection affords originator companies who create new and innovative drugs the benefits of an artificially induced, government protected, monopoly. At the bottom of our frame, exceptions to these rights, through the use of compulsory licensing and other exemptions, allow governments of insufficient scale, technology, or ability to gain much-needed drugs and leverage resources. All the while, the processes by which drug products come to market exhibit certain critical attributes which shift the optimization within the other two constraints.

A. Government Authorized Monopoly

The current legal constructs of the U.S. Patent Act and the TRIPS agreement establish protection for, and incentivize, new innovation on a national and world scale.³ The United States government provides patent protection and market exclusivity for new pharmaceutical drug products produced domestically. A majority of the countries in the world are signatories to the TRIPS agreement as part of their membership to the World Trade Organization (WTO), and they receive patent protection internationally thereunder.⁴ The U.S. government patent protection provides for a 20 year term of protection and up to an additional five years of market exclusivity to make up for the time a drug candidate spends in the regulatory review process waiting for market approval⁵. The TRIPS agreement applies to the rest of the world markets and mirrors the U.S. regulation providing twenty years of patent pro-

2. WORLD HEALTH ORG., REPORT OF THE REGIONAL DIRECTOR ON TUBERCULOSIS AND HIV/AIDS: A STRATEGY FOR THE CONTROL OF A DUAL EPIDEMIC IN THE WHO AFRICAN REGION, 6, AFR/RC57/10 (June 25, 2007).

3. See Hatch-Waxman Act, 35 U.S.C.A. §§ 156, 271 (Westlaw through Oct. 2007); Agreement on Trade-Related Aspects of Intellectual Property Rights, April 15, 2005, 33 I.L.M. 1197 (1994) [hereinafter TRIPS].

4. Understanding the WTO - Members, http://www.wto.org/english/thewto_e/whatis_e/tif_e/org6_e.htm (last visited Dec. 3, 2007).

5. *Id.*; see also *Allergan, Inc. v. Alcon Labs., Inc.*, 324 F.3d 1322, 1325 (Fed. Cir. 2003).

tection from the filing date.⁶ The U.S. government's patent protection creates a *de facto* monopoly and balances two competing policy interests: "(1) inducing pioneering research and development of new drugs and (2) enabling competitors to bring low-cost, generic copies of those drugs to market."⁷ The use of low cost licensed generic production can offer life saving anti-retroviral medications to HIV/AIDS patients and governments in the developing world that currently cannot afford to purchase originator products.

By definition, these government-authorized monopolies create a condition in which pharmaceutical companies enjoy artificially inflated market prices and comparatively higher revenues than the free market.⁸ Monopolists typically restrict output to maintain these artificially inflated prices, but even without restricted output, the monopolists' average revenue curve for the protected products becomes the industry demand curve.⁹ This means that the pharmaceutical firm will, like any firm in a competitive industry, try to maximize its profit within the constraints of the market's supply and demand curve and will capture all the demand at the optimum price.¹⁰ This pure monopolistic market model is representative of a pharmaceutical firm in a market that affords patent protection where no reasonably differentiated substitute products are available. Practically applied, no other company is producing a drug product that treats the same condition in the same therapeutic class of products.¹¹ As applied to the production of HIV/AIDS antiretroviral medication, companies can objectively set demand to maximize profits in lucrative markets without consideration for underserved or unserved markets.

In contrast, an idealistic competitive market with pure or close to pure competition will exhibit very different market attributes. The competitive market will consist of multiple firms each with small market shares, homogeneous products with seamless substitution and little or no product differentiation, low barriers to market entry, and non-collusive competitive pricing.¹² The competitive market model represents the generic drug production market where multiple firms compete in sales of bio-equivalent products.

6. TRIPS, *supra* note 3, at art. 33.

7. Allergan, 324 F.3d at 1325.

8. WILLIAM J. BAUMOL, ECONOMIC THEORY AND OPERATIONS ANALYSIS 343-346 (3d ed. 1972).

9. *Id.*

10. *Id.* at 343.

11. See generally National Institute of Health, Estimates of Funding for Various Diseases, Conditions, Research Areas, <http://www.nih.gov/news/fundingresearchareas.htm> (last visited May 1, 2007) (describing the therapeutic classes and the amounts of funding allocated to each).

12. BAUMOL, *supra* note 8, at 335-36.

Subsequently, this market model can be used to determine the market dynamics in a market where a compulsory license has been issued and the fixed cost of market entry license or patent royalties are eliminated or waived. In a competitive market, such as a generic pharmaceutical market, the price of products in the market will approach the average marginal cost of production for pharmaceutical firms.¹³ Firms will keep prices inflated enough to maintain minimal profitability; if the differential between the price and the marginal cost increases beyond the cost of entry threshold, new firms will enter the market as a result of attractive profit margins.¹⁴ This threshold can be described by the quantity, price, marginal cost, expected demand and fixed cost of market entry for a new firm in the market. Using a break-even calculation, one could see how to compute the cost benefit analysis and threshold for market entry. Later, this formula can be applied to compulsory licensing situations in establishing appropriate pricing to attract market entry for pharmaceutical firms.

V_e = expected demand of the market

$P^* = P_{be}$ = breakeven point at which price is conducive to market entry

C_v = variable or marginal cost of operations

C_f = fixed cost of entry/operations (i.e. plant and equipment)

M_s = expected market share percentage

$$P_{be} = \frac{[(V_e C_v M_s) + C_f]}{V_e M_s}$$

Note: The C_f and V_m calculations can consist of much more complex formulations including internal rate of return (IRR) and Time-Value of Money calculations as well as account for market growth and Consumer Price Index (CPI) adjustments.

When pharmaceutical firms encounter drugs that compete in the same therapeutic class and purport to treat the same disorder, albeit through a different patented substance, the market dynamic changes; the premise of product differentiation and substitution changes to allow for an overlap of the target market.¹⁵ This difference modifies the average marginal cost of the firms in monopolistic competition via product differentiation. The average marginal cost curve will not directly mirror the demand curve; however it will tangentially approach this curve.¹⁶ As applied, this model illustrates the competition between firms with products under patent protection but overlap in competitive thereptic areas or prod-

13. See *id.* at 337-38.

14. See *id.* at 338-39.

15. See *id.* at 344-45.

16. *Id.* at 345.

uct categories. For example, there are currently at least three drugs from different manufacturers to treat Erectile Dysfunction (ED); each of these products, Viagra, Cialis, and Levitra, currently receives patent protection but compete in the same therapeutic category and treat the same disorder.¹⁷ These products compete on differentiated product qualities such as dosage size, length of effect, and length of time before effects are realized.¹⁸ Similarly, there are many cocktails of antiretroviral drugs available for the treatment of HIV/AIDS.¹⁹ As is evident, the market demand for treatment sufficiently outstrips the artificially controlled supply, but products still compete based on efficacy, not on price because of artificial price supports and inelastic supply.

B. Compulsory Licensing, Least Developed and Developing Country Enforcement of Patent Rights Exemptions

On an international level, LDCs and Developing Countries receive opportunities to avoid enforcing patent rights within their countries in light of special needs such as economic, financial, technological, and administrative constraints.²⁰ Exceptions under Article 31 of TRIPS provide for provisions allowing all countries to issue a compulsory license for medicines.²¹ Some of the developed countries, including the United States, have voluntarily agreed not to issue a compulsory license, and to date, despite the overwhelming outcry for HIV/AIDS medicines in developing countries, no compulsory licenses have been issued. However, the threat of compulsory licensing, at least thus far, has provided sufficient leverage for the company seeking the license to negotiate an amicable resolution with the patent holder.²² Member countries can issue a license for virtually any reason under the TRIPS agreement and use of this flexibility is increasing rapidly.²³ Furthermore, LDCs re-

17. Press release, Harvard Health Publ'n, Two New Erectile Dysfunction Drugs: How They Measure Up Against Viagra (Dec. 17, 2003), available at http://www.health.harvard.edu/press_releases/new_erecile_dysfunction_drugs.htm (last visited May 9, 2007).

18. *Id.*

19. NGO Comment on the Attaran/Gillespie-White and PhRMA Surveys of Patents on Antiretroviral Drugs in Africa - Access to Medicines Project, <http://www.essentialaction.org/access/index.php?/archives/47-NGO-Comment-on-the-AttaranGillespie-White-and-PhRMA-surveys-of-patents-on-Antiretroviral-drugs-in-Africa.html> (last visited Dec. 3, 2007).

20. TRIPS, *supra* note 3, at art. 66.

21. *Id.* at art. 31.

22. Natasha T. Metzler, *Brazil Uses Compulsory Licensing Threat in Negotiations*, PHARMACEUTICAL EXECUTIVE, July 18, 2005, <http://www.pharmexec.com/pharmexec/article/articleDetail.jsp?id=170954>, available at <http://www.itssd.org/Publications/id.pdf>.

23. See news on current event. Dispute between Thailand and pharmaceutical manufacturer Abbott laboratories.

ceive an additional seven to ten year extension on the application of TRIPS on pharmaceutical products.²⁴ Under the threat of compulsory licensing, the markets that previously would exhibit traits of pure or differentiated monopolies will now resemble more purely competitive markets. The artificial legal barriers that normally prevent entry of copycat or generic drugs and artificially inflate the cost of entry essentially disappear under the threat of a compulsory license. Policies promoted by many of the developed countries promote free market and discourage the use of the compulsory licensing system but even the United States has used the threat of compulsory licensing to further its goals;²⁵ the United States threatened to issue a compulsory license during the post-September 11th Anthrax scares.²⁶

Under the compulsory licensing provisions and the latest interpretation of TRIPS, countries that do not possess the manufacturing capacity or technology can procure manufacturing of necessary medicines from developing or developed countries that possess such capacity. India's generic industry has been targeted to fill some of the production capacity needs for the LDCs that issue compulsory licensing. Ranbaxy is the largest producer of generic pharmaceutical products in India and one of the top ten producers in the world.²⁷ India has just recently itself started to implement patent protection based on the original exemption and application of the mailbox rule; until the point at which India began to implement patent protection, the market pricing for pharmaceutical products resembled the competitive market model using marginal costs and low or eliminated fixed costs.²⁸ Both the compulsory licensing (even though a royalty will be paid) and the exemption from enforcement of IPRs for LDCs will react according to the competitive market model, as discussed above.

According to the Doha Declaration, TRIPS does not and should not prevent members from taking necessary measures to protect public health.²⁹ Further, the Doha Declaration emphasized the

24. Jerome H. Reichman, *Procuring Essential Medicines Under the Amended TRIPS Provisions: The Prospects for Regional Pharmaceutical Supply Centers* (Oct. 17, 2006), available at <http://law.fsu.edu/gpc2007/materials/procuringessentialmedicines.pdf>.

25. See generally *id.*

26. See, e.g., *Bird Flu Prompts Call for Compulsory Licensing*, IP LAW BULL. Oct. 13, 2005, available at http://www.mhmlaw.com/media_coverage/Oct05_IPLaw_BirdFlu.pdf.

27. Ranbaxy Laboratories Limited, www.ranbaxy.com (last visited May 1, 2007).

28. Intellectual property (TRIPS) and pharmaceuticals - technical note, WTO, http://www.wto.org/english/tratop_e/trips_e/pharma_ato186_e.htm (last visited Dec. 3, 2007) (as a developing country, India had to start implementing in 2005).

29. World Trade Organization, Declaration of the TRIPS Agreement and Public Health of 14 November 2001, WT/MIN(01)/DEC/2, 41 I.L.M. 755 (2002) [hereinafter Doha Declaration].

ability for Members to use all provisions of TRIPS including compulsory licensing and favorable rules of patent exhaustion.³⁰ Compulsory licenses may be issued by any nation.

C. Declining Efficacy of Research and Development

In addition to the market constraints already mentioned, the current framework of the pharmaceutical industry experiences ever increasing costs associated with research and development along with declining efficacy of that research.³¹ The pharmaceutical industry increased spending from \$16 billion to \$40 billion between 1993 and 2004, but the number of NDA submissions to the Food and Drug Administration (FDA) has declined since 1999.³² These staggering figures lead to the current estimates which range from \$500 million to \$2 billion to produce a new drug.³³ Since the average time for a drug to traverse the discovery, development, and approval process is fifteen years, the time-value of money, interest, and opportunity cost calculations substantially impact the fixed cost of new product development for pharmaceutical firms.³⁴ The FDA makes great strides, through its critical path initiative, to improve the efficiency of its application and review processes. However, the six to ten months spent reviewing an application does not represent a significant portion of the developmental process for new drug development.³⁵ Most of the inefficiencies lie in the first three phases of clinical trial. The first two phases alone take, on average, six and a half years.³⁶ Improvements can be made in the clinical trial process and within the existing framework of the pharmaceutical drug supply chain that can help reduce these costs and improve efficiency. Additionally, government involvement in the funding of research can provide a lower effective cost of market entry for a particular drug.

III. OBJECTIVES

Moving forward within the framework of the existing pharma-

30. Reichman, *supra* note 24, at 8.

31. U.S. GOV'T ACCOUNTABILITY OFFICE, *NEW DRUG DEVELOPMENT: SCIENCE, BUSINESS, REGULATORY, AND INTELLECTUAL PROPERTY ISSUES CITED AS HAMPERING DRUG DEVELOPMENT EFFORTS* 4 (2006).

32. *Id.*

33. Christopher P. Adams & Van V. Branter, *Estimating the Cost of New Drug Development: Is It Really \$802 Million?*, 25 HEALTH AFF. 420, 420 (Mar./Apr. 2006).

34. U.S. GOV'T ACCOUNTABILITY OFFICE, *supra* note 32, at 6.

35. *Id.* at 10-11.

36. *Id.* at 6.

ceutical system several goals must be achieved through optimization. Unlike a traditional optimization, certain non-monetary, social goals must and should be achieved as a matter of public welfare while other goals must be achieved in order to ensure the survival of the industry and the continued successes of pharmaceutical firms therein. Underserved populations throughout the world experience shortages or the inability to access necessary medical treatment and care that is available and often commonplace in other regions. Throughout sub-Saharan Africa alone, over eleven million children remain orphaned as a direct result of AIDS.³⁷ The sovereigns in sub-Saharan Africa and similar regions are unable to provide for the members of their own populations and are confronted with the ever-painful struggle to gain access to medicines for their respective populations; in developed nations, the medications exist to convert AIDS into a chronic, non-fatal illness and prolong life. The U.S. and other developed nations provide billions of dollars to assist in purchasing drugs for those in need.³⁸ Frustrating as it may seem, the tremendous contributions offered by and through the U.S. and other philanthropic ventures pales in comparison to the need and demand for medicines. How can society achieve uniform access to life saving products?

In addition to funding and support of underserved populations, society needs improved efficiency in Research and Development (R&D). Firms must control and maximize the productivity of R&D efforts. Better efficacy leads to better treatments and new discoveries in underserved therapeutic classes. Society needs to lower the cost of drugs. Drug prices are a byproduct of R&D expenditures, market forces, and compound interest; the cost of chemical ingredients and manufacturing processes alone do not drive prices. Finally, and not least in importance, society must ensure the safety of patients and prevent dangerous counterfeit products from entering the market.

A. Access to Medicines

The free-market economy in which we live is challenged to devise a means by which its inherent "guiding hand" function can be induced to "lend a hand" to the underserved, disenfranchised sub-populations domestic and abroad. The question remains: "Who should be served and for what diseases?" According to the World

37. The White House, Africa Policy, <http://www.whitehouse.gov/infocus/africa/> (last visited Sept. 30, 2007).

38. *Id.*

Health Organization (WHO), essential medicines, or those given priority based on the needs of the populations, should be available at all times in sufficient quantities to avoid shortage.³⁹ Unfortunately, cost as well as unavailability of supply plagues LDCs which often have a medicine budget of less than \$30 per person, per year.⁴⁰ According to Frederick Abbott, the following describes the nature of the access to medicines problem:

The supply of essential medicines is a “public goods” problem in the sense that the private market does not adequately address it. Health care systems throughout the world require an array of low-cost medicines — some under patent by originators, some not — for distribution through public hospitals and clinics. But the provision of health care services is not limited to the public sector, even in the lowest-income countries.⁴¹

The compelling interest of capitalist economics is its derivative of profit and growth; striving to achieve bottom line results leaves little room for waste, inefficiency, or charity. Intervention is necessary to provide for those in need. Pharmaceutical firms, like other corporations of economic scale, tend to operate solely upon the principals of market demand and financial prosperity fostered from meeting product demand and market forces. As consequence will bear, these pharmaceutical firms will operate, enslaved to their investors and market forces, to serve those who can afford their products. Consequently, these firms fail to serve the needs of the economically burdensome, underserved population groups.

Contrary to market economics, it is incumbent upon society to serve the needs of all its members regardless of each member’s respective ability to pay; this does not have to be done at the cost of the firms who compete within the market, although this tends to be the traditional approach. The United States, and historically most countries and sovereigns, use taxation as a means to secure the necessary funding to service the members of its society including those disenfranchised or underprivileged members who do not contribute to the fund. Where governments fall short in providing

39. Frederick M. Abbott, *Managing the Hydra: The Herculean task of ensuring access to essential medicines in* INTERNATIONAL PUBLIC GOODS AND TRANSFER OF TECHNOLOGY, 393, 394 (Keith E. Maskus & Jerome H. Reichman eds., 2004). See also *The Selection of Essential Medicines*, WHO Policy Perspectives on Medicines No. 4 (June 2002), available at http://whqlibdoc.who.int/hq/2002/who_edm_2002.2.pdf.

40. Abbot, *supra* note 40, at 395.

41. *Id.*

necessary “public goods,” non-governmental or charitable organizations will access resources in the private markets in an attempt to fill the shortfall.⁴² Many of these public and private financial solutions fall short in the face of anomalies such as epidemic and pandemic crisis; small governments lack financial capacity to address these anomalies and rely on global resources like the Global Fund and other sovereigns like the United States.⁴³ The United States, under the Ryan White HIV/AIDS Treatment Modernization Act of 2006 and its predecessor, contributed over \$74 billion to the treatment and care the HIV/AIDS pandemic since 2001.⁴⁴

Developing countries and LDCs suffer the most from restricted access to medicines. These countries lack the resources to obtain essential medicines and face major political challenges from developed nations when threatening to invoke exceptions to intellectual property rights protection under TRIPS.

B. Research and Development Efficacy and Efficiency

Only five out of every ten thousand compounds researched succeeds during the first two stages of clinical trials.⁴⁵ Increased spending has not resulted in increased efficiency or efficacy.⁴⁶ The number of New Molecular Entities (NME) and NDAs submitted to the FDA has declined since 1996, but the spending on research has increased.⁴⁷ Concerned about the decline, the FDA commenced an initiative to reduce critical path components in the NDA approval process focusing on: (1) the number of review cycles undergone by each drug; (2) the overall time to approve and NDA; and (3) cost of development. The initiatives undertaken by the FDA aim to reduce cost through reduction in approval time; this action further signifies the importance of time-value calculations on new drug cost and pricing. After increasing research expenditures by 147%, the number of NDAs and NMEs submitted by private firms failed to grow in a similar manner.⁴⁸ Meanwhile, the number of Investigational New Drugs (IND) submitted increased.⁴⁹ These observations

42. *Id.* at 396-402.

43. *Id.* See generally The Global Fund, To Fight AIDS, Tuberculosis, and Malaria, <http://www.theglobalfund.org/en/about/aids/default.asp> (last visited Sept 30, 2007) (providing an overview of the Global Fund).

44. Press Release, Office of the Press Secretary, Fact Sheet: The Ryan White HIV/AIDS Treatment Modernization Act of 2006 (Dec. 19, 2006), available at <http://www.whitehouse.gov/news/releases/2006/12/print/20061219-4.html>.

45. U.S. GOV'T ACCOUNTABILITY OFFICE, *supra* note 32, at 6.

46. See *id.* at 4.

47. *Id.*

48. *Id.* at 12.

49. *Id.*

imply at least two things: (1) pharmaceutical firms are eliminating INDs at earlier stages in development because of more rigorous safety standards or financial considerations; and (2) the availability of good IND candidates is declining because of technological limitations on our existing research sources. Further compounding the impact of these observations, most of the NDAs (68%) submitted between 1993 and 2004 were for modifications of existing pharmaceutical products and lacked the innovation seen in new pharmaceutical drug candidates for novel therapeutic applications.⁵⁰

The efficacy and efficiency of research for new drug products is declining. The top reasons cited for this decline are limitations on scientific ability to transform discoveries into safe and effective drug products, pharmaceutical decisions about profitability of drug candidates, uncertainty about the outcome of regulatory applications, and the inability to obtain adequate intellectual property protection if available at all.⁵¹ The efficacy and efficiency of research and development must improve.

C. Need for Lower Cost of Pharmaceutical Products

During the period of patent protection and market exclusivity patented pharmaceutical products, by the nature of the industry's high research and development costs, are sometimes priced in excess of thirty times the marginal cost of production.⁵² The prices of patented products often exceed the purchasing capacity of populations in LDCs and therefore are *de facto* unavailable.⁵³ Domestically, estimates range as high as \$20 billion for potential savings through the substitution of generic pharmaceutical products for brand name patent-protected products.⁵⁴ In some respects, generic substitution allows the consumer to realize a direct price savings at the counter through lower purchase prices and lower co-pay amounts. Medicine accounts for upwards of 10% of the overall cost of health care.⁵⁵ With domestic health care costs escalating and Medicare cost overruns, a reduction in the cost of medicine is essential to the continued viability of domestic health care programs.

50. *Id.* at 17.

51. U.S. GOV'T ACCOUNTABILITY OFFICE, *supra* note 32, at 25.

52. Jerome H. Reichman, *supra* note 24, at 4.

53. *Id.*

54. EMILY COX ET. AL. 2004 GENERIC DRUG USAGE REPORT 1 (2004), available at <http://www.express-scripts.com/ourcompany/news/outcomesresearch/onlinepublications/study/gdur.pdf>.

55. PHARM. RES. AND MFR. OF AM., PHARMACEUTICAL INDUSTRY PROFILE 2007 25 (2007).

D. Safety — Reduce Counterfeiting

Safety remains a key concern in the global pharmaceutical market and, with drug counterfeiting on the rise worldwide, many LDCs are exposed to increased threats. Advances in technology, intermediary proliferation, high prices, excess demand, and a lack of international regulatory intervention fuel the escalation of counterfeiting in the pharmaceutical industry.⁵⁶ Counterfeit drugs continue to proliferate in existing pharmaceutical supply chains; the introduction of these counterfeit drugs taints the quality, effectiveness, and safety of the drug supply. Drug counterfeiting estimates range from 8% of the total drug supply in the United States to as high as 60% in other countries.⁵⁷ Counterfeiting results in lost revenues, profits and lives.

The economic impact of counterfeit drugs has a multiplicative effect worldwide. Counterfeit drugs cause substantial losses in revenue and profit, which leads to secondary effects such as law suits, insurance costs and injuries, the creation of higher prices for the end consumer, and lower profit margins for pharmaceutical companies. The “faux products” also tarnish reputations, cause costly lawsuits from adverse drug reactions, and create expensive recalls and reverse logistics expenses. Indirectly, the counterfeit products can increase regulatory and political involvement in the industry, which creates lengthened product approval times and increased costs.

Industry wide profitability for pharmaceutical companies in 1996 was estimated conservatively at 18.8%; accounting for inflation, this figure translates into \$95 billion for 2004.⁵⁸ Subsequently, estimates for lost revenue due to counterfeiting in the pharmaceutical industry were approximately 5.8% or \$29.3 billion in terms of 2004 industry profit.⁵⁹ This staggering figure represents the significant impact that counterfeit products impose on the pharmaceutical industry. The WHO estimated that the percentage of counterfeit drugs world-wide could be as high as 10%.⁶⁰

56. ALBERT I. WERTHEIMER ET AL., *Counterfeit Pharmaceuticals: Update on Current Status and Future Projections*, in BUS. BRIEFINGS: PHARMAGENERICS 2004 (2004).

57. *Id.* at 30.

58. Dr. Mahender Singh, Research Assoc. and Project Manager, MIT Ctr. for Transp. and Logistics, Supply Chain 2020 Presentation: An Overview of the Pharmaceutical Supply Chain (Nov. 16, 2004).

59. *Id.*

60. WORLD HEALTH ORG., COUNTERFEIT DRUGS: GUIDELINES FOR THE DEVELOPMENT OF MEASURES TO COMBAT COUNTERFEIT DRUGS (1999).

IV. EFFECTING A CHANGE WITHIN THE FRAMEWORK

Several forums, within the existing framework, are available to improve the access to medicines, increase effectiveness and efficacy of research, lower the cost of pharmaceutical products, and increase the safety of the products in pharmaceutical supply chains, without using price controls or otherwise diminishing the profit goals of pharmaceutical firms. Alternative mechanisms may be available through the legislative/political process. However, as proposed below, most of the goals can be reached without exercising this option. The current industry framework is not optimized within the existing constraints. The incentives provided by the government and the market do not align to properly incentivize pharmaceutical firms to maximize the use of existing resources in order to maximize profits. Additionally, within the optimization process, additional parameters can allow for the service of non-financial goals through the use of licensing constraints, rebates, or industry market pressures. This means patients suffering from HIV/AIDS in LDCs will be able to access the medicines they need while still serving the interests of all parties involved.

A. Research Reimbursements at Each Phase of Clinical Trials

Traditional market forces will dictate that reducing the cost of a product will increase the demand for a given product. Likewise, in a less elastic monopolistic market, such as the pharmaceutical market for patent-protected drug products, lowering cost will create greater profit margins under the assumption of fixed retail pricing, thereby shifting the context and perspective under which we currently view pharmaceutical firms to a view in which the pharmaceutical firm is the retailer and the university is the wholesaler. Under this perspective one can apply the principles of supply chain coordination pricing incentives to establish an optimum price under which a pharmaceutical firm can "purchase" its supplies. Assume that the price the pharmaceutical manufacturer pays for a given product is represented by the cost of licensing plus the cost of the clinical trials thereby associated. Currently, the relative cost, as seen by the pharmaceutical firm, is too high for products that treat underserved therapeutic classes or diseases. Using the simple break-even equations presented earlier, it can be determined that these product classes are lacking in sufficient market demand or, relative to profit, are too expensive to produce. In order to make one of these products attractive to a pharmaceutical firm, we must either increase the revenue or lower the rela-

tive cost. How can this be done with the current uncertainty at each phase of clinical trials?

Take into account the supply contract theory as presented by Professor Yossi Sheffi from MIT.⁶¹ Let us analogize the clinical trial phase of the pharmaceutical industry as a completely perishable process such as a newspaper stand. For the sake of argument, assume that at the end of the day, the daily newspaper has no residual or salvage value and any unsold items are waste. Similarly, assume that any NME that fails at any given stage of the clinical trial process has no salvage or residual value; once failed, the NME is essentially discarded. The wholesaler will try to sell (license) its products at the optimum price which will achieve its interests. Universities/NIH funded researchers want to push upon society as many of its achievements as possible. Meanwhile, the pharmaceutical firms (retailers) want to minimize risk and market the most profitable “blockbuster” products to maximize profit margin and revenue.⁶² Also, assume that, if all clinical trial costs were funded by the government, the pharmaceutical firms would order (license) as many products as possible since there would be relatively insignificant associated fixed costs and only marginal or variable costs of production. Analogously, if newspapers were free or provided at cost, the retailer (newspaper stand) would order a relatively large amount without consequence from risk of loss.

There is a gap between what firms are willing to pay and the combined cost of licensure with associated clinical trial expenses. Average costs at phases one, two, and three of clinical trials are \$15 million, \$24 million, and \$86 million respectively.⁶³ Many theorize that clinical trials should be funded by the government,⁶⁴ but the author posits, how much, and through what mechanism, should this be done? A proportionate distribution of risk between the two alternatives, full funding versus no funding, would produce an optimal solution within the existing framework. How do we achieve maximum efficacy for our funding? Following with the analogy, the following equations will represent the optimal “order” for the overall supply chain instead of ordering with just the retailers’ profit margin objective.

61. Yossi Sheffi, Dir., MIT Ctr. for Transp. and Logistics, Supply Contracts Presentation (Dec. 2006).

62. See *Without the Next Blockbuster Drug, Merck Faces a Murky Future*, KNOWLEDGE@WHARTON, Dec. 2003, <http://knowledge.wharton.upenn.edu/article.cfm?articleid=886> (last visited Sept. 30, 2007).

63. Adams & Branter, *supra* note 34, at 422.

64. See Tracy R. Lewis et al., *The Case for Public Funding and Public Oversight of Clinical Trials*, 4 THE ECONOMISTS’ VOICE 1 (2007), available at www.bepress.com/ev.

P = retail price
 W = wholesale price (assume this includes license royalties and associated clinical trial expenses)
 C = supplier's cost
 S = salvage value
 Q = quantity ordered
 D = actual demand
 f(D) = demand density (retail); assume market demand
 F(D) = retail cumulative demand distribution (normal)
 Q_r^* = optimal order quantity for the retailer/pharmaceutical firm
 Q_c^* = optimal order quantity for the supply channel

For this example, assume the demand distribution is normally distributed

$$F^{-1}\left(\frac{P - W}{P - S}\right) = Q_r^*$$

In contrast,

$$F^{-1}\left(\frac{P - C}{P - S}\right) = Q_c^*$$

Note: The above formulation and equations have been adapted from Yossi Sheffi's "Supply Contracts" presentation at the MIT/Zaragoza Logistics Center in December of 2006.

For the case in point, it can be generally postulated that the optimal channel order will exceed the optimal order of the firm. The optimal order for the channel, or the market demand for a given product, will, even in a relatively inelastic market, be greater than the optimal order for the pharmaceutical firm; the pharmaceutical firm (retailer) is not getting the product for free or for the same cost as the wholesaler. It is necessary to align the incentives of the pharmaceutical firms with those of the licensors' in order to achieve higher levels of market efficiency and optimality; we must align the incentives to bridge the gap between the wholesaler and the retailer.

This gap can be bridged using risk and reward preferences and the retailer's desire for profitability. It has been established that the pharmaceutical industry involves significant risk of loss at the various levels of clinical trials. Pharmaceutical firms also avoid costly trials on NMEs that serve unprofitable markets or small therapeutic classes. Risk sharing has been the key in other industries to optimize channel ordering; some have used rebate and buyback contracts for years to promote higher retail purchasing. Utilizing the previous analogy of the newspaper industry, news agencies sell papers to news stands for a given price. But in order to incentivize the news stand to carry more papers, and thereby

have the capacity to satisfy more consumer demand, the news agency will provide a buyback or salvage value to the news stand or end retailer.⁶⁵ The higher the guaranteed buyback, the larger quantity the news stand will order (limited by overall demand). By analogy, and as mentioned before, the more the government pays for clinical research (lowering the cost), the more pharmaceutical firms will take advantage and license products. This will effectively provide greater throughput and more licenses of products.

By corollary example, assume that the \$30 billion pledge from the White House to support HIV/AIDS⁶⁶ was redirected from purchasing on-patent treatment to fund university research or share the financial risk of clinical trials for new treatments. Also assume market makers require a 12.15% IRR for the pharmaceutical industry.⁶⁷ By the government sharing the risk of loss of clinical trials, 12% simple interest compounded annually on \$30 billion over an arbitrarily chosen five year term, the cost to the pharmaceutical firm for initial production of a product would be reduced by about 56%, or approximately \$22 billion. Of course, this savings would be passed to the pharmaceutical firms in the form of a rebate or incentive based on a proportion of completed product sales in the market. If we assume the annual demand for HIV/AIDS antiretrovirals is 22 million annual doses, the rebate could be structured to align industry incentives and provide higher rebates on fulfillment percentages or higher demand satisfaction. This simple example illustrates the savings and impact which would be passed on to the end consumer, and in turn, to underserved markets.

However, funding should not just be arbitrarily increased to achieve greater throughput and greater access to previously unprofitable classes. An optimal balance must be achieved and adjusted periodically to maintain proper alignment of incentives. If the demand changes, the formulation to ensure proper risk sharing and alignment of incentives must also change.

Since the risk of success at each phase of clinical trials varies by phase, therapeutic class, and a myriad of other factors, it is virtually impossible to know in advance the cost of a given clinical trial. However, after the clinical trial has been conducted it is easy to calculate a value and provide a reimbursement. This can be done through a series of at least three options: (1) rebates offered

65. Sheffi, *supra* note 62.

66. The White House, President's HIV/AIDS Initiatives, <http://www.whitehouse.gov/infocus/hiv/AIDS/> (last visited Sept. 30, 2007).

67. E. RESEARCH GROUP INC., ECONOMIC ANALYSIS OF FINAL EFFLUENT LIMITATIONS GUIDELINES AND STANDARDS FOR THE PHARMACEUTICAL MANUFACTURING INDUSTRY 3-52 (1998) available at <http://www.epa.gov/waterscience/guide/pharm/econanal/econanal.pdf>.

at each stage of clinical trials; (2) revenue sharing; and (3) option contracts.⁶⁸

Rebates are probably the most standard form of synchronizing objectives. A simple example would induce the pharmaceutical firm to spend time on certain therapeutic classes or diseases that are underserved, by providing a rebate to that firm. The pharmaceutical companies could receive a portion of their expenditures back after the completion of clinical trials. The second option, revenue sharing options, which are already used, can be adjusted to properly align goals. Right now the revenue sharing contracts are not designed to optimize performance.⁶⁹ If the universities invested more into the clinical trial process and demanded higher revenue sharing percentages, they could operate at a more revenue-neutral profit margin and also provide drug candidates that demonstrated lower risk for potential licenses. Finally, option contracts could provide an arrangement where pharmaceutical companies would pay for an option to license a drug candidate. These options could provide an upfront payment to the university in exchange for the rights to test the candidate; upon success, the firm would pay a royalty or greater percentage, based on the drug's success, to exercise the option under licensing agreement. These types of option contracts make more sense when you consider the prospect of moving the point of transition later in the clinical trial process. In this context, the point of transition is the point at which ownership of the process is transferred to the purchaser; the purchasing of a compound after the first phase of clinical trials would be less expensive than purchasing a compound after it had passed through the second phase of clinical trials. The result is less risk, less opportunity cost, and more investment in the compound.

Using a rebate model the following would illustrate the rebate amount for a given drug substance:

68. *Id.*

69. John Fraser, Executive Dir. of Commercialization, Fla. State Univ., EU-US Innovation, (April 5, 2007) (presentation available at http://www.law.fsu.edu/gpc2007/materials/EU-US_Innovation_Summit_07.ppt).

P = retail price
 W = wholesale price (assume this includes license royalties and associated clinical trial expenses)
 C = supplier's cost
 S = salvage value
 Q = quantity ordered
 D = actual demand
 f(D) = demand density (retail) assume market demand
 F(D) = retail cumulative demand distribution (normal)
 Q_r* = optimal order for the retailer
 Q_c* = optimal order for the channel
 R = Rebate amount

For this example, assume the demand distribution is normally distributed. Then

$$R = \left(\frac{P - S}{P - C} \right) W - \left(\frac{P(C - S)}{P - C} \right)$$

Note: The above formulation and equation have been adapted from Yossi Sheffi's "Supply Contracts" presentation at the MIT/Zaragoza Logistics Center in December of 2006.

This could be applied at any phase or all three phases in the clinical trial process by creating a hypothetical retailer and wholesaler at each level. Specifically, in the transition from phase two to phase three, phase two would be the wholesaler (product cost would include research already conducted) and phase three would be the retailer. Subsequently this could be used to analyze the value of the drug compound at each phase in the clinical trial process.

Overall, a system of supply chain contract coordination can be applied to achieve optimal value for both the pharmaceutical firms and those funding the initial research. By seeking optimal reimbursements, these firms can properly align their respective incentives and achieve optimality for both. University and NIH efforts to generate drugs for underserved diseases and therapeutic classes can be achieved through properly rebating and pricing the drug candidates they wish to promote.

Referring again to the \$30 billion HIV/AIDS example, the application of these new principles would imply the use of NIH funded universities to conduct and self-initiate clinical trials and further advance the involvement of research institutions beyond the current threshold of nominating or isolating NMEs. University research funding provided by NIH and alternative financing/endowment programs cost significantly less in real interest terms than monies borrowed through and for profit driven phar-

maceutical firms. Assuming that the NIH borrows money at U.S. treasury bill rates, the cost of clinical trials and the associated time-value of money would be 8-10% less than the IRR for a pharmaceutical firm. This could reduce the \$22 billion in interest costs to less than \$5 billion. This proportion of savings could be passed in the rebates given to the pharmaceutical producer or through the sale of the drug candidate after successfully completing a phase of clinical trials.

B. The Pharmaceutical Market Parity Approach

As contrary to market economics as it may seem, it is incumbent upon society to serve the needs of all of its members, but not necessarily at the expense of its own economic survival. The traditional approach to accomplish this in corporate America is taxation and government regulation. From the perspective of pharmaceutical firms, taxation is just a cost that is easily transcended upon the target markets through pricing strategies. Furthermore, regulatory impositions simply act as barriers to the production of drugs. Neither mechanism produces a direct incentive for pharmaceutical firms to serve special population groups through market economics. Actually, taxation and regulation tend to do quite the opposite, as these mechanisms foster the notion of market concentration. Firms narrow the scope of their products and services only to those markets capable of meeting their profitability goals. This is illustrated by the fact that LDCs remain underserved.⁷⁰

So how do we induce corporations to balance the scale of market economics? The answer is properly aligned incentives that do not take more through the penal nature of taxation and regulation. Accordingly, the government must give something to firms, but with a price. Currently through NIH funding, the benefits of government-funded research are made available to specific firms for products and/or services through the licensing at the university level. Right now, licensing is paid for through a system of monetary royalties and the profitability of the products at the time of licensing is often uncertain because universities don't evaluate research on the basis of profits.⁷¹ What if these pharmaceutical firms could only obtain such research in exchange for an agreement to produce and distribute other products derived from government-funded research for special interest groups? These special interest group products could include therapeutic categories, which are un-

70. Reichman, *supra* note 24, at 6-7.

71. Fraser, *supra* note 70.

derserved because they lack a sufficient size of market to warrant clinical trials. Often, potential NMEs are discarded or avoided because they target therapeutic classes of rare diseases, and the demand for rare disease therapy does not pass muster in a financial feasibility study. We could name this proposition of providing licensing based on an agreement to produce products underserved (i.e. rare disease therapeutic classes), the “Market Parity” theory and distinguish it from the traditional “Free-Market” theory of economics.

Under the Market Parity theory, we are essentially steering firms to produce and distribute their products to both profitable and non-profitable markets on the assumption that cost of the latter will be more than offset by that of the former. This offset presupposes foregone research and development costs since, at the point of licensing, these will be government-funded via NIH and university grants. As a deeper incentive to move forward with clinical trials, tax credits and deductions will be offered for risk losses and test markets of any government funded research. The success of this theory would necessitate a formulary by which the economic outcome of the Market Parity approach (M) would, in some way, equate to or exceed the value of the Free-Market approach (F); thus, if K denotes profitability then,

$$K \geq M - F$$

Under the traditional, Free-Market approach, pharmaceutical companies will generally bear all costs of R&D, as well those related to the risk of test marketing. Thus, if R_c = cost of R&D and test market costs, we can construct a typical profitability equation in which V_m = market driven demand and V_n = non-market-driven demand. We will set C_v as the variable cost of business operations, including cost of goods sold, salaries and benefits, and C_f as the fixed cost of operations. Fixed costs are assumed to be relatively equal in either the Market Parity or Free-Market approach. Additionally, assume P represents the selling price of products. In summary, the Free-Market profitability equation is:

$$F = P\Sigma V_m - (C_v\Sigma V_m + C_f) + R_c$$

The equation for the Market Parity approach is:

$$M = P\Sigma V_n - [C_v(\Sigma V_n + \Sigma V_m) + C_f]$$

The Market Parity approach foregoes R in exchange for the

variable costs associated with non-market driven demand. As a consequence, firms will not be likely to undertake and enter into any Market Parity agreement unless they can be assured that $R \leq C_v \Delta V_m$. This quantity, based upon extrinsic financial value, must demonstrate that the value forgone in exchange for marketing non-profitable, yet market-serving, products will still result in a positive net profit differential. There are also many intrinsic benefits associated with the Market Parity approach that can be quantified through a more complex model that is beyond the scope of this analysis.

Opportunity cost and the time-value of money are two of the most significant intrinsic benefits that can be realized from further calculations. Aside from the cost of resources expended to conduct research and development, there is the investment of time and the other opportunities that are conceivably foregone during this period.⁷²

The pharmaceutical industry is probably among the most suitable targets for the Market Parity approach since there are many disenfranchised population groups for which many vital pharmaceuticals are unavailable for the sake of market profitability. As mentioned before, the LDCs and many developing countries throughout the world are without access to essential medicines.

Viewing the objectives of pharmaceutical companies within the context of our Market Parity theory, suppose that government funded research projects through the NIH and universities derived a cure for the common cold. Suppose also that the government offers license agreements to pharmaceutical companies for this cure. However, instead of paying a traditional royalty or license fees as originally described, the pharmaceutical firm must produce certain other non-profitable therapeutic class products in exchange for the license. Alternately, as a condition of licensure, the company could be required to distribute or license an authorized generic to serve LDCs elsewhere in the world. Other alternatives could be used as compensation that would fulfill non-market goals and objectives of the government and university systems. A \$1 billion producing "blockbuster" drug could be licensed in exchange for the research and production of three drugs which would only breakeven or lose revenue annually. These drugs, however, would achieve political and humanitarian objectives by serving underprovided therapeutic or disease classes.

Again, through the illustration of the HIV/AIDS example, some

72. David R. Henderson, *The Concise Encyclopedia of Economics*, <http://www.econlib.org/LIBRARY/Enc/OpportunityCost.html> (last visited Nov. 9, 2007).

of the \$30 billion could be used to incentivize a pharmaceutical firm to produce more of the antiretroviral drugs using the Market Parity approach. However, rather than providing monetary funding or rebates, additional license opportunities could provide firms with profit opportunities. A firm could receive a license to produce an originator ED drug with an estimated \$2 billion a year market in exchange for producing two million annual treatment doses of antiretroviral medication at 3% over the marginal cost of production.

C. NIH/University Licensing Standards

One of the many non-legislative tools that can be used to effect a change in the industry is the adaptation of existing licensing standards. University licensing standards and the licensure of research produced from NIH funding can be modified in a manner that properly incentivizes pharmaceutical firms to “do the right thing.” The licensing of research is quite probably the best forum through which to implement the aforementioned Market Parity theory. As a practical application of the Market Parity theory, pharmaceutical firms would receive bundles of drug candidates or drug candidate classes on which to conduct clinical trials and proceed to market. Obviously, with less than .01% of NMEs reaching the phase three clinical trials, it is very difficult to predict which drug candidates will be successful and which ones will not. However, one can determine the target populations and markets for diseases. Therapeutic classifications of diseases can be broken into segments of the population. Currently there are more than six thousand rare diseases that affect approximately twenty-five million Americans; globally there are far more people afflicted.⁷³ By approximating based on market demand for a given therapeutic class or particular disease, one can approximate the gross revenue there associated as the price multiplied by the non-market demand, PV_m . Once determining the profit potential for a given therapeutic class, the university licensing system can bundle products or research results to create a portfolio of candidates which will give an estimated rate of return for a pharmaceutical licensee.

Through the use of the portfolio approach, an approach utilized throughout the financial services industry, the pharmaceutical firms would realize better stability of revenue streams. When products go off-patent, these companies would rely on a more di-

73. PHARMACEUTICAL INDUSTRY PROFILE 2007, *supra* note 56, at 10.

versified portfolio of products in a wider variety of therapeutic classes to support revenue and offset the losses in years where patent protection on blockbuster drugs is lost.

Further application of market theory shows that the HIV/AIDS example would not only benefit from the exchange of licensing for blockbuster drugs but also could benefit the pharmaceutical firm through bundling, by providing a portfolio of underserved therapeutic classes of drugs bundled together. Before a university is willing to license a blockbuster drug, it must bargain for minimum production quantities of antiretrovirals at much lower profit margins, or even losses, to offset the benefits derived from licensure of a single \$1 billion drug over a fifteen to twenty year exclusivity period.

D. Supply Chain Activity Improvement — Improving Efficiency of Research and Development

Once a drug compound receives regulatory approval it can still take upwards of one full year for the product to reach the market. The raw material for some pharmaceutical products takes over a year to traverse the supply chain and become a finished product. Processing and distribution comprises less than twenty-five days of the lead time.⁷⁴ The industry needs more than ever to improve and expedite the process of launching new products. According to Forrester Research's calculations, the per-day cost in lost sales for a \$1 billion drug is \$2.74 million.⁷⁵

The location of [new drug] launches affects how quickly doctors and patients can access the most advanced treatments. One study shows that the U.S. averages a [four] month delay from initial drug launch to market. In Europe, this delay ranges from [seven] to [nineteen] months.... The reason: lengthy reimbursement negotiations that follow government approval of any new drug.⁷⁶

The pharmaceutical industry experiences a high level of scrap and rework in manufacturing processes. The industry average for rework and discarded product is 50%. Rework and scrap cost compa-

74. Singh, *supra* note 59.

75. UNITED PARCEL SERVICE, *Building Supply Chain Capabilities in the Pharmaceutical Industry*, UPS SUPPLY CHAIN SOLUTIONS 4 (2005).

76. PHARM. RES. AND MFR. OF AM., PHARMACEUTICAL INDUSTRY PROFILE 2005 20 (2005).

nies millions of dollars. Estimates place the cost of a scrapped batch of product around \$3-4 million.⁷⁷ The industry is also notorious for maintaining high levels of work in progress (WIP) and finished good inventory. WIP inventories of up to 100 days are not uncommon.⁷⁸ Pharmaceutical inventories in the U.S. have nearly doubled in the last decade and are approaching record high levels estimated around \$18 billion.⁷⁹

E. Ensuring Safety — Counterfeiting and the Radio Frequency Identification Safety

One of the future challenges for the pharmaceutical industry involves the combating of counterfeiting. The FDA has recognized that Radio Frequency Identification (RFID) technology possesses potential to reduce the threat of counterfeit drug introduction. The FDA believes, “[m]odern electronic technology is rapidly approaching the state at which it can reliably and affordably provide much greater assurances that a drug product was manufactured safely and distributed under conditions that did not compromise its potency.”⁸⁰ As the FDA continues to examine alternatives to act against the counterfeiting pandemic, “[RFID] tagging of products by manufacturers, wholesalers, and retailers appears to be the most promising approach to reliable product tracking and tracing.”⁸¹ Additionally, “[a]uthentication technologies for pharmaceuticals have been sufficiently perfected that they can now serve as a critical component of any strategy to protect products against counterfeiting.”⁸² If the FDA imposed mandatory implementation of RFID, the industry on a whole could experience vast changes in the cost basis for supply chains.

Although the pharmaceutical industry would take a significant cost hit to implement the new technology, the end result, if counterfeiting were reduced, would create substantial savings and additional profit. Presently, the average price to the consumer of a bottle of prescription medication is estimated at around \$53.10. It is estimated that 76% of that profit is received by the manufacturer (\$7.60), while the wholesaler receives 3% (\$0.30), and the other 21% is retained by the retailer (\$2.10).⁸³ According to the

77. Singh, *supra* note 57.

78. *Id.*

79. *Id.*

80. FOOD AND DRUG ADMIN., COMBATING COUNTERFEIT DRUGS, ii, (2004) available at http://www.fda.gov/oc/initiatives/counterfeit/report02_04.html.

81. *Id.*

82. *Id.*

83. Singh, *supra* note 57.

previous calculations and estimates, almost \$3.10 of profit is lost per bottle due to counterfeiting.

The cost of the infrastructure to implement RFID would be a one-time sunk cost. However, the benefits would continue to contribute to the bottom line. Even if the cost of the RFID tags, which is where the main portion of the cost exists, remained high at \$.20 per tag, the benefits would still show significant increases in profit from the reduction in counterfeit products. The benefits of RFID implementation far outweigh the costs.⁸⁴

In addition to the quantitative losses suffered by the pharmaceutical industry, the world also experiences immeasurable humanitarian losses as a result of counterfeit drug introduction. In China, about 192,000 lives were lost (cumulatively) throughout 2001.⁸⁵ The benefits of RFID seem promising in the pharmaceutical industry. The implementation may pose challenges, but with the backing and possible subsidy of regulatory agencies, these great giants of the pharmaceutical world may gracefully adopt the new technologies.

F. The Bargain

As discussed, the participants in the pharmaceutical industry in the U.S. market can take advantage of the Market Parity approach and the Supply Chain Channel Coordination theories to achieve optimality in the domestic market. This application can extend to the underserved populations of LDCs, while still allowing the pharmaceutical firms to maintain a certain degree of autonomy and control over their products. As Jerome Reichman illustrated, there are advantages of collective or regional bargaining practices that can produce benefits for underserved or least developed regions.⁸⁶ These countries can form regional supply and demand centers that are more attractive to pharmaceutical firms that previously would not serve small regions.⁸⁷ Currently the regional committee for Africa is exploring opportunities to engage in collective bargaining agreements and regional bulk purchasing of essential medicines including antiretroviral drugs used in the treatment of HIV/AIDS.⁸⁸ However this application of economies of

84. Mike D. Lagasse, IBM Consulting Services, Presentation at the First Canadian RFID Conference: RFID in the Supply Chain (2003).

85. Wertheimer et al., *supra* note 55, at 32.

86. See generally Reichman, *supra* note 23.

87. *Id.*

88. See WORLD HEALTH ORG., REPORT OF THE REGIONAL DIRECTOR ON LOCAL PRODUCTION OF ESSENTIAL MEDICINES, INCLUDING ANTIRETROVIRALS: ISSUES, CHALLENGES AND PERSPECTIVES IN THE AFRICAN REGION, 4, AFR/RC55/10 (2005).

scale should not be limited to the purchasing side of the supply chain.

Utilizing the Market Parity theory to mandate drug licenses into packages that are issued contingent upon other production fulfillment, universities can also work collectively to provide more weighty and substantial bargaining authority. When universities bind together to license multiple potential blockbuster drugs into a package with many drugs that serve unprofitable disease categories the outcome will produce economic bargaining scale. Pharmaceutical firms will not be able to license drugs for fractions of a percentage, instead they will need to fulfill other non-market demand which otherwise would have been overlooked. The economic scale gained through collective bargaining will have similar supply side results as the proposed regional bargaining for purchases.

Additionally, universities can establish blackout regions or markets where the licenses are not effective. University licensing can exclude LDCs which the licensor would not have otherwise served. This licensing can also include more creative provisions, similar to those proposed in Reichman's paper, whereby pharmaceutical companies have the option to produce the products for the underserved regions at a price close to the marginal cost of production.⁸⁹ The price can be set to establish a profit margin above the marginal cost of production, and using the breakeven equation presented earlier in this paper can produce an optimal market entry price that will serve the underserved population.⁹⁰ These countries, although not required to do so yet under TRIPS, can offer premature patent protection for the products generated for the region. Along with early assurances and use of a "breakeven plus margin" approach, these regions can attract larger pharmaceutical companies to produce genuine products at marginal profit margins. These breakeven equations would not incorporate the research and development costs associated with the region since the pharmaceutical company would not have served the region and did not account for sales in the region to offset these costs in their projections.

Underserved sovereigns and regions can also attract pharmaceutical production activities to serve their respective markets through the use of tax incentives. Pharmaceutical companies produce drugs in at least three stages. Because of the nature of the pharmaceutical industry, specifically the extremely high profit margins relative to marginal cost, the pharmaceutical companies

89. See generally Reichman, *supra* note 21.

90. See generally *id.*

will usually manufacture products in various different countries to take advantage of tax havens and different taxing law benefits in each unique production location. These companies rely on proper planning and transfer pricing in order to maximize production. Countries like Ireland, Puerto Rico, Brazil, and Benelux have offered such taxing incentives to attract major pharmaceutical production operations.⁹¹ Since pharmaceutical companies must pay taxes in each region based on exports and transfer pricing, countries can provide substantial savings when high differentials in transfer pricing exist and low cost of labor makes conversion of pharmaceutical ingredients relatively inexpensive.

Of the [forty-six] countries in the African Region, [thirty-eight] have pharmaceutical industries; [thirty-five] have secondary level production and [twenty-five] have tertiary production (some countries having both secondary and tertiary production). Eight countries have no such industry. South Africa performs all types of local production, including primary production of chemicals and limited local production of generic active (pharmaceutical) ingredients. Generally, the majority of the production facilities are privately-owned; locally-produced medicines are mostly generic and satisfy only a small proportion of national requirements.⁹²

The existing production facilities can be expanded or purchased by larger pharmaceutical firms and used in market expansion in the region.

Tax incentives and proper transfer pricing can be used to take advantage of beneficial tax laws and exemptions. This can be cultivated to generate a domestic pharmaceutical market and better serve the now underserved region. It is also notable to mention that as the CPI or equivalent metric grows in the now underserved regions, profitability outcome calculations will change. As these countries and regions grow over the next twenty years, these markets, now relatively small, could grow into substantial revenue centers for pharmaceutical firms. The voluntary promise of early intellectual property rights protection and the ability to gain market share in an emerging region may be sufficient to attract even

91. Personal interviews with industry experts at Novartis in Basel Switzerland as well as other industry contacts in the MIT Supply Chain 2020 project.

92. WORLD HEALTH ORG., *supra* note 87, at 2.

the most reluctant pharmaceutical producer.

V. CONCLUSION

The legal and social framework establishes a representative model within which the existing domestic and global markets operate. The model establishes the constraints, and application thereof, to the participants in the market. Pharmaceutical firms act on profit motivation and aim to achieve high levels of research and development efficiency as it relates to revenue generation and cost savings. Universities and the NIH achieve research advances through the use of public funding and achieve medical advances across a broad spectrum of therapeutic categories and diseases. Meanwhile, developing and least developed countries, as well as underserved therapeutic classes, endeavor to gain access to essential medicines and promote fruitful developments on behalf of their respective afflictions.

General social welfare improvements in access to medicines, advancements in research and development, safety procedures, and political leverage can be achieved through a series of optimization techniques. Without the use of legislative remedies participants can improve their respective positions and objectives within the existing framework. Philanthropic or socially driven organizations can improve access to medicines domestically through the use of the Market Parity and optimization approaches in order to incentivize pharmaceutical companies to produce drugs for underserved diseases and therapeutic classes. These organizations can achieve risk-sharing with pharmaceutical firms and find optimal reimbursement schemas for each target therapeutic category. These incentives do not have to be monetarily or financially-oriented rebates; rather, these can be structured licenses where social non-market goals are achieved. The bargaining power of organizations entering into licensing agreements can be bolstered through the use of collective bargaining or source aggregation where universities present drug development packages to pharmaceutical companies including a portfolio of products. Least developed or underserved regions and countries can achieve improved access to medicines through a combination of threats and rewards including compulsory licensing, tax incentives, and collective regional bargaining. Further, using optimization techniques, pharmaceutical firms and licensors can share costs and risks at each stage of the clinical research process to ensure maximum throughput, efficiency, and efficacy in drug research; the gap between respective interests will be closed and better market (financial) and

non-market (social) demand fulfillment will ensue.

Pharmaceutical manufacturers can take advantage of supply chain techniques to lower work-in-progress inventories, development times, waste, and time-value of money costs associated with research and development. Finally, the safety of each pharmaceutical product in the market can be improved through the use of RFID technology to reduce counterfeit products as well as the secondary effects and losses related.

Right now \$30 billion buys \$30 billion worth of medication, far less than is required to serve all twenty-two million HIV/AIDS sufferers. Through the use of techniques illustrated in this paper, a \$30 billion initiative will provide multiple times the market value of that amount in derived benefit and quantity of treatment dosages. Through application of Market Parity, rebates, collective bargaining, responsible and bargained university licensing, and further supply chain optimization, the effect of any contribution will be amplified; the industry will prosper and the market and non-market needs of all parties will be satisfied.

Overall, through the application of the techniques listed above, the industry participants can maximize efficiency and achieve greater objective success throughout the existing framework. These changes can be effected faster than legislative proceedings and can provide near optimal results within the existing framework.