PERPETUAL PATENTS FOR PHARMACEUTICALS – ARE THERE ANY WELFARE JUSTIFICATIONS?

by

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ABSTRACT

Patents have been an important motivation for innovation. Innovation is an important source of economic growth. One of the primary objectives of the patent system is to reward innovators by giving them certain monopoly rights. Principles of Economics textbooks point to a consensus among economists that patent protection serves as a barrier to entry. Such a barrier stifles or limits competition, gives exclusive rights to the patent holder, and results in emergence of monopoly power. Creating monopoly rights for the patent holders, in general, gives profit maximizers the incentive to innovate. The public generally understands this tradeoff, and thus the concept of patent protection is an issue that finds acceptance universally. In the light of this, increasing criticism of the pharmaceutical patent protection seems to be out of context. This criticism possibly results from the lucrative financial performance reflected through balance sheets. However, the pharmaceutical industry needs to be viewed as different in two distinct ways: first, pharmaceuticals should be treated differently from other regular commodities when it comes to patent protection since they deal with life and death tradeoffs, and thus should fall in a unique category. Second, the pharmaceutical industry faces a problem of ‘copycat’ products where imitators come out with parallel formulations in the form of generics, by slightly altering ‘processes’ and thus bypassing ‘product’ patents. Here the Research and Development of one firm is imitated relatively easily by using slightly different processes to synthesize therapeutically similar chemical entities. The alternative processes mainly focus on lowering costs. These cheaper generics compete with the
patented products, thus affecting their sales and profitability, and in turn impacting the ability of the patent holder to recover the huge R&D investments.

This thesis hypothesizes that, there are economic and welfare justifications for having perpetual patents on pharmaceuticals. Perpetual patents can pave the way for lowering drug prices in the short and long-run, leading to greater affordability to a larger cross-section of the population. Additionally, perpetual patents allow the firms to spread out their cost recovery over a longer time horizon, instead of trying to recover the R&D costs in a much shorter window, thus keeping prices lower. Perpetual patents would also provide a disincentive for the proliferation of generics, which will sustain profitability of patent holders, and this is likely to induce pharmaceutical firms to invest larger amounts to ongoing research.

The paper looks at data for the last two decades on R&D investment in general and on Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS) drugs or vaccines by the five top pharmaceutical firms involved in this field of research, and correlates that with the mortality rates in this time period. The paper analyzes the implications of reduced patent protection on the pharmaceutical industry in terms of a sustained lowering of ‘real’ investment in R&D and the impact of this in the general health scenario of any nation. The paper also looks at how this influences the development pipeline of newer drugs, and the consequences of substantial delays in this process on the population mortality rates. The paper concludes the empirical analysis, by
tying up these aspects in the context of their impact on societal welfare, and suggests policy options which can be explored to maximize social welfare without compromising on future drug development.
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LIST OF ABBREVIATIONS

CES – Constant Elasticity of Substitution
FDA – Food & Drug Administration (United States)
FTC – Federal Trade Commission
HIV/AIDS – Human Immunodeficiency Virus/ Acquired Immune Deficiency Syndrome
IND – Investigational New Drug
LDC – Least Developed Country
NCE – New Chemical Entities
NDA – New Drug Application
NGO – Non Governmental Organization
NIH – National Institutes of Health
NME – New Molecular Entities
PhRMA – Pharmaceutical Research and Manufacturers of America
PLC – Product Life Cycle
R&D – Research and Development
TRIPS – Trade-Related Aspects of Intellectual Property Rights
UN – United Nations
UNAIDS – Joint United Nations Programme on HIV/AIDS
WHO – World Health Organization
CHAPTER I

INTRODUCTION

Pharmaceuticals invariably play a vital role in maintaining the health status of the population of any economy. Without a disease-free and healthy workforce, achieving productivity goals and ultimately economic growth may be a planner’s nightmare. Pharmaceutical drug therapies have traditionally supplemented nutrition, public hygiene, and medical care, as methods for preserving health. The available drugs find use in treating existing diseases and conditions, whereas at the same time newer drugs are discovered to treat previously unknown or emerging diseases. In spite of these successes and its important role in the economy, the pharmaceutical industry is facing increasing criticism and scrutiny on the issue of continued patent protection for both emerging drugs and processes. One of the reasons for increased focus and scrutiny of the pharmaceutical industry is because of the general perception of high levels of profit associated with this industry. A second reason relates to the continuous mergers and acquisitions in the industry seen in the current and past decades. This has led to the creation of ‘mega’ pharmaceutical corporations, and resulted in concentration of monopolistic power in the hands of a few pharmaceutical firms. Reduced competitiveness has stoked the fear related to the notion of welfare loss to the society through monopoly pricing tendencies. This is because the lack of competition and concentration of power within a few firms can affect the business practices, in terms of the firm’s ability to price discriminate, impacting the availability and affordability of medications to the patients who need them the most.
Patents can be interpreted as exclusive property rights, and their existence depends on the extent of their enforceability within certain territorial or sovereign state boundaries. A patent by definition is a property right granted by a sovereign state to the inventor of a novel, non-obvious, and useful invention.

Whatever patent strategy is employed by the inventor, the aim is always the same – to maximize the profit accruing to the inventor and those who have supplied him or her with the capital necessary to develop and commercialize the invention. While public funding of the training of scientists and basic research vastly expanded the understanding of human pathology, it was the profit motive, operating through pharmaceutical firms accountable to investor shareholders, which provided desperately needed funds to discover the new therapeutic regimens for patients. By the decade of the 1980s, patent dependent pharmaceutical firms developed more than 92 percent of all the new drugs.

Patent rights are limited in duration, with the global standard being 20 years from the date of application and they work differently in different industries. This time period equally applies to pharmaceuticals, where the patent system provides protection against generic competition for about 20 years from the date of first filing for a patent. In the United States, patents can be extended only for half the time period consumed by the regulatory approval process, and for a maximum effective patent term of fourteen years¹. Further, the legislation restricts the exclusive right of use which normally accompanies the patent

¹ 35 USC Sec. 156
grant by permitting generic competitors to use the product for testing and developing the
generic alternative while the patent is still in effect, which further impacts the effective
patent term. This in turn permits a generic product to be marketed virtually the moment
the patent expires. Regarding non-exclusivity of patents in certain industries, we can look
at the electronic industry, as an example, where patents are generally shared among
competitors through pooling or cross licensing. This sharing becomes inevitable and
necessary, because a given product often contains many patented technologies.

On the other hand, the pharmaceutical industry is a technology based industry in which
the patent normally equals the product, and a patent protects the extensive investment in
R&D, including clinical testing and other pre-launch regulatory requirements, that are
required before the product can be offered in the market. A distinguishing characteristic
of production in the pharmaceutical industry is the considerable ‘upfront expenditure’
necessary to research the molecule and then scale-up to construct the new commercially
viable production plant. Including the opportunity costs of foregone capital payments,
R&D accounts for 30 percent of the costs of a new product in the research-based
industry. Moreover, an additional 40 percent of total expenses account for marketing,
administration, and inventory costs. In the end, only 25 percent of total production costs
are actually related to the direct manufacture and distribution of the pharmaceutical
product.
The research process for new drugs is daunting. The average new drug entails up to $800 million to develop, while the generic costs less than $2 million. Development time for a new drug averages over 15 years. This long development time gives less opportunity during patent life to collateralize investment, and most efforts at innovations fail. Less than 1 percent of the chemical entities that are examined in the pre-clinical period actually reach the human testing stage, and only 20 percent of these gain Food & Drug Administration (FDA) approval. Nor is patent protection so protective of price: a study of 148 new drugs in the U.S. found that only 13 had no close substitutes. In fact, most new chemical entities in the 1980s and 1990s generated insufficient revenues to cover the development cost. Faced with a portfolio of occasional winners, pharmaceutical companies must collateralize their investments in R&D by charging higher prices for the successful drugs that actually make it to the market. This means, some portion of the price of the newly marketed drug pays for the costs of many failures. On top of that, the remaining effective duration of patent protection after the drug hits the market, as discussed earlier, literally forces the pharmaceutical firms to be in a mad rush to recoup the investments – leading to charging of higher prices. Given the nature of this research ‘lottery’, it is too simplistic to comment that a particular drug is priced too high because its revenues exceed related costs by a considerable margin, as depicted in the firm’s current balance sheets. The following excerpt on pharmaceutical R&D spending throws some additional pointers on this issue.
R&D Spending in Context

Although the general perception is that R&D spending is the main driver in pharma costs, manufacturing is in fact a more significant part of the cost picture. For the 16 biggest pharmaceutical companies, 2001 sales totaled $300 billion and costs were about $250 billion, according to Raymond Scherzer, GlaxoSmithKline’s vice president – engineering for global manufacturing and supply. While manufacturing-related expenses represent 36%, or $90 billion, of the $250 billion in costs, R&D represents only 16%, or $40 billion. Material costs represent roughly half of all manufacturing costs, Scherzer claims.2

Another common misconception is that promotional spending is greater than R&D investment. In 2000, however, industry’s total promotional outlay, including value of free drug samples provided to physicians, was about $15.7 billion, compared to $26 billion for R&D, according to the Pharmaceutical Research and Manufacturers of America (PhRMA).3

In the context of the above discussions, patent protection for pharmaceutical products is especially important compared with other industries, because the actual manufacturing process is often easy to replicate, and can be copied with a fraction of the investment than that required for the research and clinical testing. Expenditures on pharmaceutical research increased from $0.94 billion in 1974 to $38.8 billion in 2004. Much of this increase represented a shift of investment from Europe, where increasingly burdensome

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price controls have threatened investors’ return on capital. This shift is reflected by the fact that in the year 2003, 78.6 percent of the R&D investment by global pharmaceutical companies was in the United States, versus 21.4 percent elsewhere, including Europe. The extensive cost required to produce a new pharmaceutical product has meant that private sector investment in pharmaceutical innovation has been disproportionately directed to products meeting the needs of patients in developed countries, particularly the United States, which combines strong patent protection with a market free of price controls. Under such a scenario, it may be reasonable to assume that an analysis of patent protection mechanisms, R&D spending by the five top pharmaceutical firms engaged in anti-HIV/AIDS drug research in the United States, and related mortality rates may well be a valid representation of the overall situation, and a starting point of a study, or a series of studies, justifying the need to seriously consider the case for perpetual patent protection on pharmaceuticals. Obviously, the scope of such a study is definitely very wide, encompassing other pathological conditions and drugs related to these. That effort will also be undertaken in the future, and will attempt to substantiate the outcomes of this current study.

The pharmaceutical industry has another important characteristic that sets it apart from other industries that require patent protection. In many technology-based industries, it is possible to keep inventions a secret until the moment they are marketed. This enables the inventors to delay patent filings until the last possible moment and, therefore, to maximize the effect of the 20-year patent term which runs from filing of the patent
application. In the culture of medical research and pharmaceuticals, however, emphasis is placed on early disclosure of inventions, usually long before the final product can be placed in the market. This is because of the fact that scientists working in the field of human pathology have an obligation to share their findings as soon as possible with their peers so that those peers will be able to benefit from the new knowledge in their own research. Additionally, unlike the electronics or software industry, the pharmaceutical industry is heavily regulated by government agencies to assure the safety and efficacy of products that will be sold to customers. The lengthy time-period between patent filing and placing the product in the market means that the pharmaceutical manufacturers receive far shorter periods of patent exclusivity than is the case for other patent dependent industries.

One question that may naturally arise in the context of such a patent regime is: “Will perpetual patents stifle further basic drug research?” In other words, will such perpetual patents lead to complacency and lethargy in the respective pharmaceutical firms, thus affecting ongoing investments in basic research? To address this issue we may take the help of the concept of the Product Life Cycle (PLC) approach, (Figure 1). A drug or new chemical entity (NCE), like any other product, will approximately go through the phases of Development, Introduction, Growth, Maturity, Decline and Withdrawal.
The duration of each of the phases in the PLC subsequent to the preliminary ‘Development’ phase will depend on the uniqueness of the molecule, its efficacy and safety profile, the patient affordability and acceptance of the drug regimen, pricing structure, ongoing availability or non-availability of newer or better molecules, the geographical marketing reach of the firm – collaborations, co-marketing arrangements, etc., marketing strategies and the financial capabilities to sustain promotional efforts over a period of time, the absence or presence of side-effects in the Post-Marketing Phase IV stage, regulatory interference, and various other related matters. So, no matter how good a molecule is it will ultimately go through the various phases of the PLC, and reach the ‘Decline’ and ‘Withdrawal’ phase. Depending on the attributes just mentioned, a new drug might be in the market for a long period of time, or a relatively shorter term. Non-investment in further basic research by pharmaceutical firms will lead to a scenario where a drug, because of its PLC becomes obsolete, and the firm does not have a viable alternative product to replace it. This will seriously jeopardize the firm’s revenue stream,
and ultimately the survival of the firm. So, in spite of perpetual patents, any firm will have to continue to invest in basic R&D, and have replacement products in the pipeline to ensure that it stays competitive and continues to operate.

Thus, under these circumstances, to maintain a competitive edge, overall profitability of the firm and portfolio of offerings in the market, any firm even at the bare minimum will have to keep innovating and offering newer and better products. This follows from the fact, that regardless of how good a product or a molecule is, and the PLC any molecule faces, basic human endeavor will always be to discover a better product, which will surpass the attributes of the currently available offerings. One of the reasons for this is that almost all drugs have some inherent drawbacks. Thus, there will always be ongoing research, subject to available funds and stakeholder interest, to discover even better molecules, as part of the research process. This will keep up the competitive pressure on the patent holder to stay abreast, and channelize a certain amount of investment in discovering newer drugs.

Another point worth a mention is that we are looking exclusively at the role of private investments, specifically investments made by the pharmaceutical industry by ploughing back a percentage of net profits, when we talk about investment in basic research and overall R&D investments in this thesis. We are deliberately excluding the amounts invested by any government department, quasi-government institutions, or various science and technology foundations. Only a passing mention of government or quasi-
government investments will be used for the sake of comparison of the dollar volume of investment in R&D in basic pharmaceutical research, and this thesis does not intend to dwell in-depth on this issue. This is done to primarily focus on investment as a ‘private good’, as opposed to including R&D investment as a ‘public good’ option.

Turning to the other side of the coin, we look at the evolution of new drug molecules that are discovered to treat various existing or emerging diseases. For the purpose of this thesis, as mentioned earlier, we will look at only one such “disease”. There are various reasons for this, and just a few are mentioned here. One primary reason is to keep things simple. So, we test empirically the relationship between patent length and welfare in only a single case in this thesis. Second, we intend to extend a similar type of analysis for other pathological conditions, in subsequent extensions of this paper, to see if this relationship holds universally, and can be used to substantiate the argument for extending patents infinitely. Third, the underlying logic being similar, in the case of other drugs and diseases, the additional empirical studies will try to reinforce the justification for pharmaceutical patents in perpetuity. Fourth, as per UNAIDS, the Joint United Nations Programme on HIV/AIDS, the current scenario of AIDS infected patients is explosive and alarming, and increasing to endemic proportions. The number of people living with HIV has risen from around 8 million in 1990 to 33.4 million in 2008, and is still growing (please refer to Appendices 1 to 1.5). This, therefore, is a global medico-health crisis, and pharmaceutical drugs have a critical role to play in helping mankind to come out of this scourge. In this context, we turn to one of our current killer diseases of the 21st century,
and explore how a perpetual regime can provide the impetus for additional investments for newer drug discoveries.

We, therefore, step back and look briefly at the background of one of the “killer diseases” in this current century, as mentioned earlier, known as Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS). Initially the condition was first reported around 1981 in *Morbidity and Mortality Weekly Report* under the quiet title of “*Pneumocystis* pneumonia – Los Angeles”\(^5\). By December 2000, 21.8 million people worldwide had died of the disease. The HIV/AIDS epidemic has caused many to question whether a stronger global patent regime creates new obstacles to meeting public health emergencies. The controversy over non-availability of patented therapies for the treatment of HIV/AIDS in the countries most affected, which happen to be also the “poorest” in terms of being able to afford the costly & patented therapies, has resulted in renewed interest in patent protection and on the subject of compulsory licensing of pharmaceuticals. In the context of the various rounds of World Trade Organization (WTO) negotiations, and the efforts to find some form of agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), the debate has focused on the access to medicines in developing countries. These countries have been concerned that the WTO’s patent rules do not give them enough flexibility to adequately address public health concerns in the explosive spread of HIV/AIDS cases.

One of the major requirements of the TRIPS agreement is that WTO member states may not discriminate among technologies in providing patent protection, which meant that exceptions to patent protection in many countries for pharmaceutical products must be eliminated. The industrialized countries, on the other hand, are concerned that broad exceptions to patent rules would undermine intellectual property rights. Until the TRIPS Agreement in 1994, many developing countries provided no patent protection on pharmaceuticals. While countries that have joined the WTO have obligated themselves to provide such protection, Least Developed Countries (LDCs) are not required to meet this obligation until 2016. The continuing lack of patent protection up to this time makes it very difficult to establish research-based industries in most developing countries. This lack of patent protection in LDCs is manifested in a distinct reluctance on the part of major research based pharmaceutical firms making the patented products’ available to these countries. This non-availability of such medicines has resulted in higher mortality rates of the general population in spite of the existence of at least some form of treatment.

After two years of discussion, the WTO Council affirmed that the TRIPS Agreement permits such compulsory licenses in health emergencies. However, to date no compulsory licenses have been actually issued, even though the threat of compulsory licensing has been used as a means of seeking lower prices. A major danger in compulsory licensing is that it will further discourage the commercial research and development (R&D) necessary for new drugs which are needed to fight global epidemics such as HIV/AIDS, or any other disease for that matter. Another danger is that compulsory licensing can be used to seek price levels below what a given national market
is capable of supporting, further concentrating the burden of pharmaceutical innovation on developed countries like the United States, and discouraging development of drugs targeted specifically at the disease burdens of countries using compulsory licenses.

The focus of this paper is an empirical analysis, not a theoretical one. This is in spite of the difficulty in obtaining research and development data related to the individual pharmaceutical firms, as these are regarded as proprietary information, and as such the firms are totally reluctant to share these beyond their individual corporate boundaries. The study has had to settle mostly for whatever data was accessible, and available in the public domain, and was constrained by this handicap.

This paper is developed in the following format. Chapter 2 reviews the existing literature in the area of patents, with particular reference to pharmaceuticals. Chapter 3 develops the simple model used as the basis of this study and endeavors to relate the implications of patent protection, drug development time, HIV/AIDS mortality rates and welfare. Chapter 4 looks at the empirical evidence, and how such evidence relates to this thesis proposal. Based on this analysis, Chapter 5 discusses the current and emerging scenarios, and suggests possible policy approaches that can be useful in tackling the issues involved. This chapter then concludes by summarizing the study and outcomes.
The issue of patents has been debated in various forums, and evoked a considerable level of interest and discussion in various literatures over the years. The pioneering work of Nordhaus, on relationships between inventions, patents and welfare, sets the tone for future discussions, by developing a model in which patent length determines the size of innovation. Here, the optimal patent length is the one which induces an innovation of welfare-maximizing size. However, almost all of these and subsequent discussions in this vein have been mainly confined to patents, in general. Though there have been references to infinite life patents in general in many studies, as we shall see later, any discussions or literature with exclusive focus on the impact of possible pharmaceutical patents in perpetuity, and the likely impact of such a patent regime on societal welfare, has been conspicuously missing. Inferences from the study of patents in general have been used as pointers, in terms of their applicability to the pharmaceutical patents, but even here they have remained largely confined to the theoretical aspects of the impacts of short versus long term patents. There is a distinct lack of adequate empirical studies on the impact of long term pharmaceutical patents on welfare. As mentioned earlier, the difficulty in obtaining proprietary data on R&D investments of pharmaceutical firms to test any hypotheses, or conduct empirical studies, may be responsible for a vacuum in this area. On the other hand, whatever scant literature that is available in terms of extending patent life, or longer patent protection for pharmaceuticals, tend to come out with conflicting
conclusions. A vast majority of the studies related to pharmaceutical patents have shown some perspective of compulsion, possibly undertaken with the latent motivation of meeting regulatory requirements. The pharmaceutical firms probably felt obligated to undertake these studies, to substantiate their pricing claims, and to get the drug to the market as early as possible. This makes it all the more important to focus on an investigation from a relatively neutral perspective. Thus, as in this case, no individual firm is involved in sponsoring such a study, and the results reflect on the pharmaceutical industry as a whole. The outcome of such a study can be used to formulate an unbiased policy perspective about patent length, which ultimately will have an impact on overall societal welfare.

Even though we do not see specific studies which attempt to correlate long-term impacts of perpetual pharmaceutical patents on welfare, we do come across a few studies related to the issues of time-span of pharmaceutical patents and monopoly power, the impact of patent length on the rate-of-innovation, longer patents and their implication in lowering imitation barriers, the crowding-out effects of longer patent duration, the indicators and determinants of market power in the multinational context of the pharmaceutical industry, etc. We look at a few of these studies to get a feel of the ongoing debate, and the different approaches and perspectives that have evolved. For example, Tandon, examines the concept of optimal patents in the context of putting a check on monopoly power, by bringing in a policy of compulsory licensing. The paper shows, under certain simplifying assumptions, that optimal patents will have an indefinite life, for both process and
product innovations, and may lead to substantial welfare improvements. This thesis is explores patent length of pharmaceuticals in a similar vein, but here the approach is empirical, rather than a theoretical one. On the other hand, Horowitz and Lai in their study identify the patent length that maximizes the rate of innovation, and compare that with the patent length that maximizes consumer welfare. Their model suggested, that the patent length that maximizes the rate-of-innovation, exceeds that which maximizes consumer welfare, because they claim that increases in patent length, have countervailing effects on the size and frequency of innovation. In other words, the authors claim that a longer patent length increases the size, but decreases the frequency of innovation, and thus advocate a non-extension of patent length. Rather they suggest a patent length that will maximize welfare, and they try to show theoretically this is not an indefinite patent length, but some length of time where patent duration and maximization of welfare match. We can see that this conclusion of Horowitz and Lai seems to run counter to what Tandon proposes in his paper.

Again, looking at patents in general, in a study on the crowding out effects of longer duration patents Chou and Shy demonstrate the impact of long duration of patents, and how such patents affect investment in new product development. The authors approach this by constructing an overlapping-generations model of saving, investment, and product innovation, which when confronted with the issue of longer duration patents, seem to compete with the younger generations’ savings, rather than investment in new product development. Even though the patent system is essential for growing economies, the
authors’ premise is to counteract the common belief that long duration patents, leads to longer duration monopolies, which in turn increases the incentives of the firms for product development in the economy. The authors do this by showing the impact of an increased number of monopoly firms on savings, leading to a crowding out effect on further investment. It is interesting to note that this study shows the difference between finite and infinite patent length patents becomes insignificant in the face of very high population growth rates. However, this discussion is again on patents in general, and the length of the patent duration, rather than any reference or applicability to the specific pharmaceutical industry scenario.

Statman and Tyebjee, on the other hand, bring in the concept of brand loyalty in the discussion on pharmaceutical patents, which they claim tends to extend the patented drugs competitiveness by a few more years even after patent expiration. However, they also point that such competition of off-patent drugs with generics, is at the expense of innovation in the drug industry.

Gallini warns against taking a uniform approach towards all patents, and advocates that there should be different approaches to specialized technologies. As mentioned earlier in the introduction, pharmaceuticals may fit the bill of specialized products or technologies, which need to be viewed differently from a more generalized patent process. Waterson, points out that giving monopoly rights through patents is socially desirable because it leads to encouragement of innovation. On the other hand understanding the welfare
effects of this monopoly power is problematic, and it is difficult to alter patent law to make it industry specific. This thesis’s basic premise, on the contrary, is to propose such a pharmaceutical industry specific patent regimen.

Levin highlights the “free rider” problem as an outcome of weak patent protection, which in turn limits the incentive for innovation. Conferring ‘property rights’ in the form of patents, provides the incentive to engage in inventive activity. The author goes on to point out that all the issues raised by U.S. firms in recent years regarding infringement of patent rights on a global context are almost exclusively confined to chemical and pharmaceutical patents. This again brings to focus the urgency associated with protecting and enhancing the pharmaceutical patent regimen.

In an empirical study on patents and innovation in general, Mansfield takes a random sample of 100 U.S. manufacturing firms, and the results reinforce the aspect of high dependency of patents in certain industries, mainly the pharmaceutical and chemical sectors. In fact, this study shows that over 80 per cent of patentable inventions are patented in the pharmaceutical and chemical industries, and this is important to these industries for survival and progress. Mansfield’s results go on to reinforce earlier studies in this respect by Taylor and Silberston, who used data from 27 firms, and showed that 60 percent of pharmaceutical R&D was dependent on patent protection. Similarly, Mansfield, Schwartz, and Wagner, using data from 48 product innovations, found that 90 per cent of pharmaceutical innovations would not have been introduced without patents,
and the pharmaceutical industry regards patents as much more important, than many other industries.

Heller and Eisenberg explore the ‘anticommons’ approach to biomedical research to see if patents can deter innovation. Garrett Hardin introduced the metaphor “tragedy of the commons” in Science in 1968, which postulates that people often overuse resources they own in common, because they have no incentive to conserve. The metaphor overlooks the possibility of underuse when governments give too many people rights to exclude others. The authors conclude that policy makers should seek to minimize restrictive licensing practices which interfere with downstream product development and ensure coherent boundaries of upstream patents.

Griliches uses patent statistics to illuminate the process of innovation and technical change. Among the major findings of the study was the discovery of a strong relationship between patent numbers and R&D expenditures in the cross-sectional dimension, implying that patents are a good indicator of differences in inventive activity across different firms. While the propensity to patent differs significantly across industries, the relationship between R&D and patents is close to proportional, especially for firms above a minimal size. The author goes on to mention, that the practical implication of these findings is that in the absence of detailed R&D data, the much more plentiful patent data can be used instead as an indicator of both, inventive input and output.
Since patents have an impact on the availability and affordability of products throughout the world, Penrose takes a look at the impact of patenting inventions in the less-developed countries (LDCs), by local inventors. The author accepts that there are advantages for a LDC in protecting its own inventors, from having their ideas and inventions taken over by foreign firms without their consent and without compensation. In this case, the firms which take over such patents will primarily use these to enhance the monopoly position of the foreign patentees in the local market or as a means of transferring funds or facilitating restrictive practices. In this context, it might be worth mentioning about the attempts of certain firms of trying to patent Basmati rice, or other spices and condiments such as turmeric, and many traditional herbs, which have been available for centuries in many LDCs or developing countries. These efforts, for the time being, have not met with much success because of vigorous resistance and legal filings from the concerned countries, but at least gives an indication of what Penrose is trying to point at.

Kadidal examines the approach to pharmaceutical biodiversity resources in the context of Rio\textsuperscript{6} patents. However, approaching this issue without considering how LDCs might extract the maximum economic rents from biological diversity ignores the sizeable global efficiencies and the welfare benefits for Third World nations that would result from the full redistribution of these rents.

\textsuperscript{6} The Earth Conference: Biodivisive, ECONOMIST (U.S. Edition), June 13, pp. 93-94.
Gilbert and Shapiro, looking at patents in general, and not specifically at the pharmaceutical sector, suggest that the conventional analysis of optimal patent length, based on the tradeoff between the incentives for innovation and the extent of static monopoly dead-weight loss, has been misplaced, or at least takes too limited a view of the instruments that make up “patent policy.” When patent policy is viewed to be a choice of patent breadth as well as patent length, the authors find that the optimal length may easily be infinite. In their analysis in the paper, Gilbert and Shapiro provide a general condition for the optimal length of patent grant to be infinite. The most important limitation of this study is the assumption that the underlying environment is stationary, and this assumption is made to focus on a single innovation.

Judd, provides the basis for the study of patents in an economy with a continuum of goods, and examines the case where the utility function was symmetric and with constant elasticity of substitution (CES). Using the CES utility function, the author then investigated an economy where not all goods were patented. Since infinite life patents on all goods achieve the social optimum in this case, any loss in efficiency with finite-life patents and incomplete coverage is due to these limitations. Judd found that finite-life patents may cause unstable development, and could possibly explain observed periodic behavior in innovation.

In another paper, Gallini puts forward a different argument on optimal patents in the context of imitation products. The author extends the theory of optimal patents to allow
for costly imitation of patented innovations. Since imitation is assumed to be costly in this paper, a rival’s decision to imitate depends on the length of patent protection awarded to the patentee, with the argument, that the longer is the patent life, the more likely that the rival is going to ‘invent around’ the patented product. Gallini argues that extending patent life, therefore, may not provide the inventor with the increased incentives for research or to patent the innovation. These results are, obviously, in sharp contrast to other results suggesting optimality of narrow, infinitely long patents. Strongly contrasting Gallini’s perspective, Klemperer explores the trade-off between a patent’s length (its lifetime) and its width (scope of coverage), and suggests that a wider patent generally reduces the distortion of consumers’ choices between the patented brand of the product and the unpatented, lower priced varieties sold by competitors. This also allows for higher prices of the patented products, which increase (relative to profits) the deadweight losses from consumers switching consumption out of the product class. Klemperer shows under what conditions infinitely lived but very narrowly focused patents are the socially efficient way to reward innovation, and under what conditions very short-lived but very broad patents are optimal.

Lerner examines the relationship between patenting behavior and different litigation costs, and looks at various legal aspects of patents. The author shows that, firms with high litigation costs appear less likely to patent in the same subclass as rivals, and these firms seem particularly reluctant to patent after awards to firms that have low litigation costs. The paper also contributes to the understanding of the patenting process. It does
this by looking at the effectiveness of patent protection which has received little empirical attention despite its importance in several theories of socially optimal patent policy. The theoretical analysis of the impact of costly litigation also raises questions about the recent shift to stronger patent rights. Coming somewhat closer to pharmaceuticals, in another paper, Lerner examines whether patent scope affects the valuation of new biotechnology firms. Since this is another rapidly evolving sector, though we do not focus on this in the present thesis, Lerner first develops and validates a proxy for the breadth of patent protection based on the International Patent Classification scheme. The study finds that patent scope has a significant impact on firm value, in manner consistent with theoretical suggestions.

Heywood looks more broadly at drug access, patents and global health in the context of the July 2000 General Comment by the UN Committee on Economic, Social and Cultural Rights. The paper focuses on a wider definition of health, and the resultant implications for governments, multinational pharmaceutical companies, and people in the context of previously unknown diseases, including HIV and AIDS. Global health is assessed according to the extent of global access to patented life-improving medicines. Kamien and Zang use a model to explain a more recent tactic introduced by pharmaceutical firms, where they introduce generic substitutes for their own branded products before their patents expire. This can be construed as a roundabout way to extend and hold on to the monopoly power conferred by patents. By this early introduction, a branded product’s
provider seeks to establish a Stackelberg leadership role in the forthcoming generic substitutes market. However, despite its Stackelberg leadership position, the firm’s branded product’s price declines for a sufficiently large number of entrants into that market, even though total producer profits are higher than they would be, if the branded products’ suppliers had not been involved in supplying their own generic substitute. One possible approach suggested by Danzon and Towse relates to economic case for patents, while continuing with the practice of differential pricing to increase affordability of on-patent drugs in developing countries while preserving the incentive for innovation. Differential pricing, based on Ramsey pricing principles, the authors suggest, is the second best efficient way of paying for global joint costs for pharmaceutical R&D.

Interesting and somewhat contradictory outcomes were found by Sakakibara and Branstetter, when they studied the available evidence from Japanese patent law reforms of 1988. The authors raised the question ‘Does an expansion of patent scope induce more innovative effort by firms?’ When they studied the Japanese patent reforms of 1988, it was found from interviews with practitioners and available professional documents for patent agents, that the reforms significantly expanded the scope of patent rights. However econometric analysis using both Japanese and U.S. patent data on 307 Japanese firms

7 The Stackelberg leadership model is a strategic game in economics in which the leader firm moves first and then the follower firms move sequentially. It is named after the German economist Heinrich Freiherr von Stackelberg who published Market Structure and Equilibrium (Marktform und Gleichgewicht) in 1934 which described the model. In game theory terms, the players of this game are a leader and a follower and they compete on quantity. The Stackelberg leader is sometimes referred to as the Market Leader.
found no evidence of an increase in either R&D spending or innovative output that could plausibly be attributed to patent reform. However, taking a look at the contexts of compulsory licensing and patent protection in Canada, Pazderka, finds that after almost two decades of compulsory licensing of prescription drugs, when Canada restored full patent protection in two legislative steps taken in 1987 and 1992, the outcome was quite the opposite of the Japanese experience. Inter-industry comparisons of R&D spending trends within Canada, inter-country comparisons of R&D spending trends within the pharmaceutical industry, as well as trends in Canada’s share of foreign R&D spending of US-owned multinationals suggest a statistically significant increase in Canadian pharmaceutical spending after 1987.

Analyzing the impact of patents on firm performance, Bloom and Van Reenen show that patents have an economically and statistically significant impact on firm-level productivity and market value. While patenting feeds into market values immediately it appears to have a slower effect on productivity. Grabowski and Vernon discuss the approach towards patent life extensions in the context of the 1984 Drug Act (Drug Price Competition and Patent Term Restoration Act). The adverse impacts on pharmaceutical R&D of the 1962 Kefauver Amendments to the Food, Drug, and Cosmetic Act, have been a significant factor underlying increasing R&D costs, longer gestation periods, and shorter patent terms for pharmaceuticals. The 1984 Act would only increase patent life up to five years. The basic advantage of the Act was to make generic producers face less restrictive and stringent approval processes, whereas the original patent holder did not get
any significant benefits. In another paper, Grabowski and Vernon address the impact of the repeal of the anti-substitution laws in over forty states on dispensing of patented brand name products. The law allows pharmacists to substitute generic products, unless a physician specifically insists on a brand name product. Grabowski and Vernon also estimate the effects of regulation in the U.S. ethical drug industry which has been characterized by a number of adverse developments. This has led to a sharp decline in the rate of new product introductions, and the incentive for engaging in R&D activity. This to a great extent is because of the rapid increase in costs and the risks involved in developing new products.

Turning to the aspect of mergers that have become the norm in the pharmaceutical sector, to better manage R&D budgets, Graves and Langowitz in their study show, that firms in the pharmaceutical industry experience decreasing returns to scale in R&D as the level of R&D expenditure rises. Their study suggests the wave of mergers in the industry may yield less innovative productivity than expected, because of a strong correlation R&D budgets and firm size. On the other hand, Angilley’s analyses of two international samples of pharmaceutical companies covering virtually the complete size range, yielded consistently significant correlations between innovative output on the one hand, and firm size and R&D expenditure on the other. This is very different from the conclusion arrived at in the study by Graves and Langowitz. A different outcome is put forward in Jensen’s paper where the study shows that firm size does not significantly affect the marginal productivity of research expenditures. Henderson and Cockburn come out with results
which are in contradiction with what Jensen concluded. Henderson and Cockburn examine the relationship between firm size and research productivity in the pharmaceutical industry. Using detailed internal firm data, the authors find that larger research efforts are more productive, not only because they enjoy economies of scale, but also because they realize economies of scope by sustaining diverse portfolios of research projects that capture internal and external knowledge spillovers. In pharmaceuticals, economies of scope in research are important in shaping the boundaries of the firm, and it may be worth tolerating the static efficiency loss attributable to the market power of large firms in exchange for their superior innovative performance.

Rounding off the literature survey with a brief look at the welfare aspects of patent protection, Deardorff in his theoretical study uses a simple model of invention and patent protection to examine the welfare effects of extending patent protection from the country where the invention has taken place, to another country that is only a consumer of the patented products. Deardorff shows that, while the welfare of the inventing country certainly rises with the extension of patent protection, that of the other country probably falls, and may well fall by more than the increase in welfare of the inventing country. In particular, as patent protection is extended to a larger and larger portion of the world, the effect on the welfare of the world as a whole of extending it to the rest of the world becomes negative.
As can be seen from the above, fairly extensive review of some of the available literature, which mostly deal with patents in general, and not always specifically pharmaceutical patents, various divergent views emerge on the welfare aspects of longer term patents, relative to the prevailing patent regime that exists as of now. This incongruence of approaches and the resultant contradictory conclusions or opinions as to the duration and welfare benefits that can accrue from longer duration patents, leads one to think if a fresh and more radical approach is warranted to give a different perspective to this debate. Most of the work in this context relates to the longevity of patents and how that impacts various facets of innovation, and are theoretical in scope. The frequency and extent of innovation is then used as a benchmark, or a proxy for changes in welfare. In light of such divergent studies and outcomes, it is thus all the more imperative to take another critical look at the aspect of patents in perpetuity. Prompted by this divergence of approaches and views, this study looks at pharmaceutical patents specifically, to see if there can be real welfare gains, in not only national level of healthcare, but welfare improvements in terms of global healthcare, by having infinite duration patents, and if policy options in this regard need a thorough re-examination.
CHAPTER III

THE MODEL

The approach of our model is kept as simple and intuitive as possible, and built on the basic premise that reduction of mortality implies increase in welfare. However, in the case of this paper we are looking only at reduction in mortality based on treatments using specific drugs available. Since we are focusing on a specific pathological condition, i.e., the case of reduction in mortality of HIV/AIDS, we are primarily analyzing cases using available drugs or drug cocktails. We are not looking at other causes of reduction in mortality, e.g., preventive measures, educating the target audience on safer sex methods, governmental or non-governmental support programs, etc. So, in effect we are assuming other factors to be constant, or *ceteris paribus*, and looking at the scenario in a partial equilibrium perspective. Thus, we consider only one of the major factors that this reduction of mortality is directly related to, which relates to the drugs or drug cocktails available at that point of time. In this study we are more interested about the drugs which are in the development pipeline, the time it is taking to develop these drugs and the time period it might take for these drugs to be made available in the market. All these factors will be directly influenced by the firm size, firms’ capability to sustain their R&D investments and the actual trends of R&D spending. The lower the R&D investment, the more prolonged the time taken to develop the therapies, and the lower the probability of any drug reaching the market at an early date. In our empirical analysis, we are more
concerned at the real investment in R&D, in addition to the nominal R&D investment trends. Depending on the nominal and real investment trends, as well as the R&D investment volume in dollar terms, we can get the picture of how much of the investments are being actually channelized in new drug discoveries.

We look at the concept of welfare in the context of specific therapies available, and start off with the basic premise discussed earlier – that reduction in mortality using drug therapies available, implies increase in welfare. We can write this intuitive approach as:

Change in Welfare = Change in Mortality + Number of Drugs Available + Other related factors

\[ \Delta W_t = \Delta M_t + D(A) + \alpha \]

where, \( W_t \) = Welfare at time \( t \), \( M_t \) = Mortality at time \( t \), and \( D(A) \) = Number of Drug therapies available, or drug availability, at that point of time. The drug availability will depend on the incentives the firms have in terms of investment in R&D based on research time, Approval period, and how quickly the R&D investments could be recovered. This can be summarized as:

Drug availability = Research time + Drug approval/introduction + Recovery period of R&D Cost + \( \alpha \)

\[ D(A) = R(t) + D(I) + C(R) + \alpha \]

where\( D(A) \) = Drug availability, \( R(t) \) = Research time, \( D(I) \) = Drug introduction, and \( C(R) \) = Recovery period for research cost. This recovery period for research cost is currently the time limits imposed by the prevailing patenting regulations. Firms try to recover as much as possible of the R&D investments in the short window they have when they actually market the drug after all necessary approvals and clearances. Perpetual
patents will directly impact this R&D investment recovery period to a much longer time horizon, which in turn should have a direct impact on lower initial drug cost. What we must remember, however, that even if patents can be held in perpetuity, the competitiveness of the pharmaceutical sector, ongoing discoveries of new molecules, the product life cycle, etc. will prod the firms to recover the investments as early as they can – but, in this scenario, the market is playing the role of ‘innovation motivator’, rather than any government intervention. We can write the recovery period of R&D investments as:

Recovery period of Research Cost = Available Patent Years + Marketing costs + $\alpha_3$

$$C(R) = P(Y) + C(M) + \alpha_3$$  \tag{3}$$

Combining (2) and (3), we have:

$$D(A) = R(t) + D(I) + P(Y) + C(M) + \beta$$  \tag{4}$$

where, $\beta = \alpha_2 + \alpha_3$

This in other words means that drug availability $D(A)$, is directly dependent on the times related to research period $R(t)$, the introductory period $D(I)$, patent availability period $P(Y)$, and marketing costs before and after introduction $C(M)$.

From (1) where we had:

$$\Delta W_t = \Delta M_t + D(A) + \alpha_1$$

We can substitute equation (4) for $D(A)$, and re-write equation (1) as:

$$\Delta W_t = \Delta M_t + R(t) + D(I) + P(Y) + C(M) + \beta$$  \tag{5}$$

When we talk of patents in perpetuity, we are implying:

$$P(Y) \to \infty, \text{ i.e., } P(Y) \text{ becomes very large}$$

This implies that the R.H.S. of equation (5) becomes very large $\Rightarrow$ Change in welfare ($\Delta W_t$), the L.H.S of the equation, also becomes very large for the equality condition to
hold. This, therefore, shows that welfare changes significantly with increasing the patent period.

At this point, in the context of equation (3) above, it is worth mentioning what Nordhaus mentions on the optimal life of patents should be:

“As patent lives are lengthened (or shortened), the amount of invention increases (or decreases). What are the considerations that determine optimal life of a patent? As the life is increased, two opposite forces affect the level of economic welfare. First, a longer patent life increases invention and thus gives on balance a larger amount of output for a given level of inputs. This is a positive effect. Second, a longer life means that the monopoly on information lasts longer and thus there are more losses from inefficiencies associated with monopoly. The optimal life of a patent is that point at which the two forces balance at the margin.

In determining the optimal life it is necessary to assume a social welfare function to be maximized. As we are dealing with individual industries, the most useful measure of social welfare is net surplus (consumers’ plus producers’ surplus less resource cost). To determine the optimal life, the welfare function is maximized with respect to the life of the patent.”

What is worth noting in this comment of Nordhaus, is his assertion that longer patent increases invention, which may be translated into increase in welfare, by implication. However, the second issue that Nordhaus raises about monopoly on information needs to be addressed in the context of competitive pressures in the market as well as the Product Life Cycle concept. The inventive process in pharmaceuticals (like any other inventive

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8 Nordhaus’s footnote: This welfare function suffers from several well known shortcomings. It is necessary that the marginal utility of income is constant, which means among other things that the industries examined form only a small part of the economy. Income must be optimally distributed among agents in the economy and the changes in the life of the patent must not change the distribution from its optimum. If these conditions are not met, the conditions for the optimal life change.
process) will continuously throw up newer drugs and molecules, through different processes, on which the firm may not have monopoly on information. These will directly impact the competitiveness, profit margins, and marketability of any product, and firms will have to keep investing on R&D in an ongoing basis to survive in the market. The question that needs to be addressed is related to the ‘dollar volume’ of R&D investments that will take place, and this will be directly impacted by the firm’s size and profitability, as well as the resultant discoveries that are made and the times required to make these discoveries. Higher R&D investments should in all probability lead to faster discoveries as well as larger number of newer molecules.
CHAPTER IV
EMPIRICAL EVIDENCE

To begin with, we start by looking at the evidence in empirical terms and overall pharmaceutical R&D investments over the last three decades. In this context, to get a realistic view of actual investment, we will look at the trends in both nominal and real terms (base period 1967). Since we are primarily focusing on the R&D investments in the U.S., we will look at all the empirical data and R&D trends in the context of the ‘The Drug Price Competition and Patent Term Restoration Act of 1984’, usually referred to as the Hatch-Waxman Act of 1984. This act was designed to promote generics while leaving intact the financial incentive for continued investments in R&D. It allows generics to win FDA marketing approval by submitting bio-equivalence studies (as opposed to clinical data, which is costlier to compile). It also grants a period of additional marketing exclusivity to make up for the time a patented pipeline drug remains in development. This extension cannot exceed five years, and it is in addition to the twenty years exclusivity granted by the issuance of a patent. Another provision of the Hatch-Waxman Act grants a 30-month stay to drug companies that file suit against generic manufactures that challenge their patents. This has become controversial in recent years,

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9 In the Senate of the United States, June 10, 2003, Mr. Gregg (for himself, Mr. Schumer, Mr. McCain and Mr. Kennedy) introduced (6/23/1983) the following bill which was read twice and referred to the Committee on Health, Education, Labor and Pensions. A Bill entitled the “Greater Access to Affordable Pharmaceuticals Act” (Hatch-Waxman Act of 1984) was titled ‘A bill to amend the patent laws of the United States’. The latest major action: 9/24/1984 Became Public Law No: 98-417. Related bills: H.R. 2610, H.R. 3605.
as pharmaceutical companies have used the provision to keep generics off the market by protecting their drugs with extra patents of poor quality, filing lawsuits to protect the patents even when the lawsuit will be lost, but getting the extra market exclusivity anyway. However, we need to note, that though the Hatch-Waxman Act gives a little additional leeway to the patent holder pharmaceutical companies to recover their R&D investments, (effectively 20 years + extension of 5 years maximum + a 30 month stay where applicable) it’s a small step forward in the direction of achieving perpetual duration patents, as this thesis proposes. It will be interesting to see the impact of this Act, on R&D investments in the U.S., and may be helpful in supporting or disclaiming any claim that longer term patent protection in fact will provide the incentive for larger investments in R&D. This in turn is expected to lead to more frequent and innovative drug discoveries – thus having available a bigger repertoire of available drugs to tackle current and emerging diseases. When looking at the various graphical trends, one dotted vertical line is used to distinguish the time period up to 1984, and then another vertical dotted line around 1990, for the period 1984 – 1990 and beyond. This will give us some perspectives and insight into the effects related to the Hatch-Waxman Act. There have been continuous efforts from FTC, FDA, senators, industry groups, NGOs, etc. to modify the original Act – some towards making the entry of generic drugs easier, and some to ensure that the pharmaceutical houses are given adequate incentives to continue to innovate.
We will further look at the break-up of the R&D trends for the domestic U.S. scenario and R&D trends abroad, as well as the annual sum total of both of these investments. The reason for making this distinction and looking at domestic U.S. R&D investment and R&D investment abroad separately, as mentioned earlier, is because of the shift in investment from Europe to the U.S in the 1970s. Europe’s increasingly burdensome price controls had threatened investors’ return on investment, and this was evidenced in the fact that in 2003, 78.6 percent of the R&D investment by the global pharmaceutical companies was in the United States, versus 21.4 percent elsewhere, including Europe. Strong patent protection in the U.S., combined with a market free of price controls, has been the primary motivator for this shifting of investment.

Figures 2.1 and 2.2 show the nominal and real R&D spending trends, respectively, for the period 1970 – 2005. The spending figures are given in terms of billions of US$. (The 2005 figures were estimates wherever available.) As can be seen from these aforementioned figures, domestic U.S. R&D investments show a fairly sustained growth trend both in real and nominal terms. The difference between real and nominal investments is in terms of the value of R&D investments in billions of US$. The real investment shows an increase between 1984 and 2005 of US$ 4.42 billion (460.5% growth), whereas the nominal investment shows an increase of US$ 28.46 billion (954.3% growth). Looking now at the increase in investment for the same period, 1984 to 2005, for R&D investments abroad, the real investment increased from US$ 0.192 billion to US$ 1.365 billion (610.94% growth), and in nominal terms from US$ 0.5964 billion to
US$ 7.9871 billion. However, both in real and nominal terms, the volume of investment in the U.S., far exceeds the R&D investment abroad for the same period.
Figure 2.1 Nominal R&D Investment

Figure 2.2 Real R&D Investment
In Figures 3.1 and 3.2, we look specifically at the domestic U.S. component of nominal and real R&D spending. Again, we see an increasing trend in both nominal and real terms, though the point worth noting, as before, is in terms of investment in dollar terms. The dollar value of investments in real terms, have been significantly less than what the nominal values portray, even though the overall trends are similar.
Figure 3.1 Nominal Domestic U.S. R&D spending

Figure 3.2 Real Domestic U.S. R&D spending
If we factor in the Hatch-Waxman Act of 1984 into this time span (the vertical dotted line around 1984), it does show an interesting trend in the pre-1984 period versus the post-1984 period. It is fairly obvious from available data, that the R&D investment trend in the pre-1984 period was fairly stagnant. The trend starts changing in the post-1984 period, i.e., post Hatch-Waxman Act period. If we look further at the additional 5-year period as the Act envisages (thought, at this point, not considering the additional one-time 30-month stay provision), there can be seen a fairly sustained trend in increased R&D investments as we look at the post-1990 scenario. This by itself may be just one pointer to the fact that prolonging patent duration not only has a positive impact on inducing additional investments, but an even longer term patent duration will sustain this process. It will also provide the pharmaceutical firms a longer time span to recover their R&D investments, without the threat of generics coming in. The ability to spread their cost recovery over time will not force the firms to recover these costs in a hurried way by charging high prices in the near-term, before the patents expire. This will by itself allow the pharmaceutical firms to charge lower prices right from the initial launching and marketing phases, making the new drugs more affordable, which was by default the aim of the Hatch-Waxman Act in terms of helping lower-cost generics get into the market. In fact, under such a scenario the necessity for generics will not be felt, as the patent holder firms themselves can market the by-product of their own research at more affordable rates. This, obviously, will have a clear positive impact on societal welfare because reaching the masses will lead to higher production and further economies of scale.
Figure 4.1 Comparison of Nominal Domestic U.S. & Abroad R&D

Figure 4.2 Comparison of Real Domestic U.S. & Abroad R&D spending
In Figures 4.1 and 4.2, we superimpose the R&D spending abroad on the domestic U.S. spending, and make a comparison of domestic U.S. R&D spending with similar R&D spending abroad, both in nominal and real terms. As we saw in the earlier figures, the trends are similar, though the difference primarily lay in the dollar volume of investments. However, in the context of the Hatch-Waxman Act, which was directed to the U.S. market, there is hardly any impact on the R&D spending abroad, and there is fairly muted growth in the R&D spending abroad.

It might be interesting to take a recent snapshot of R&D spending for 2004 vs. 2005 for a few top pharma companies. Figure 1 provides the picture. The listing includes five of the top firms involved in HIV/AIDS drug or vaccine research, viz., GlaxoSmithKline, Merck, Bristol-Myers Squibb, Abbott and Roche.
Table 1: R&D spending at Top Pharma Comparison: 2004 vs. 2005

<table>
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<tr>
<th></th>
<th>2004(N)</th>
<th>2005(N)</th>
<th>% Growth (N)</th>
<th>2004(R)</th>
<th>2005(R)</th>
<th>% Growth (R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer</td>
<td>7.7</td>
<td>7.4</td>
<td>-3.9</td>
<td>1.4</td>
<td>1.3</td>
<td>-7.1</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>5.2</td>
<td>6.3</td>
<td>21.2</td>
<td>0.9</td>
<td>1.1</td>
<td>22.2</td>
</tr>
<tr>
<td>GlaxoSmithKline*</td>
<td>5.2</td>
<td>5.7</td>
<td>9.6</td>
<td>0.9</td>
<td>1.0</td>
<td>11.1</td>
</tr>
<tr>
<td>Novartis</td>
<td>4.1</td>
<td>4.8</td>
<td>17.1</td>
<td>0.7</td>
<td>0.8</td>
<td>14.3</td>
</tr>
<tr>
<td>Merck*</td>
<td>4.0</td>
<td>3.8</td>
<td>-5.0</td>
<td>0.7</td>
<td>0.6</td>
<td>-14.3</td>
</tr>
<tr>
<td>Astra Zeneca</td>
<td>3.5</td>
<td>3.4</td>
<td>-2.9</td>
<td>0.6</td>
<td>0.6</td>
<td>0.0</td>
</tr>
<tr>
<td>Eli Lilly</td>
<td>2.7</td>
<td>3.0</td>
<td>11.1</td>
<td>0.5</td>
<td>0.5</td>
<td>0.0</td>
</tr>
<tr>
<td>Bristol-Myers Squibb*</td>
<td>2.5</td>
<td>2.7</td>
<td>8.0</td>
<td>0.4</td>
<td>0.5</td>
<td>25.0</td>
</tr>
<tr>
<td>Wyeth</td>
<td>2.5</td>
<td>2.8</td>
<td>12.0</td>
<td>0.4</td>
<td>0.5</td>
<td>25.0</td>
</tr>
<tr>
<td>Abbott*</td>
<td>1.7</td>
<td>1.8</td>
<td>5.9</td>
<td>0.3</td>
<td>0.3</td>
<td>0.0</td>
</tr>
<tr>
<td>Roche*</td>
<td>4.9</td>
<td>5.4</td>
<td>10.2</td>
<td>0.3</td>
<td>0.3</td>
<td>0.0</td>
</tr>
<tr>
<td>Schering Plough</td>
<td>1.6</td>
<td>1.9</td>
<td>18.8</td>
<td>0.3</td>
<td>0.3</td>
<td>0.0</td>
</tr>
</tbody>
</table>

N – Nominal
R – Real

* Involved in HIV/AIDS drug/vaccine research

From Table 1, we can see that the largest pharmaceutical company, Pfizer, did not record any growth in R&D spending. Of the five largest companies involved in HIV/AIDS drugs/vaccine research, only GlaxoSmithKline and Bristol-Myers Squibb had recorded a growth in R&D spending. Two others, Abbott and Roche did not show any growth in spending in real terms, though there was some nominal growth. Merck, in fact showed a decrease in R&D spending both in real and nominal terms. This chart may give an indication as to why the new drug inventive process has not been able to provide an array of marketable and effective newer therapies in the market.
As discussed earlier, increasingly burdensome price controls and other restrictions in Europe, lead to a shifting of the R&D investment from Europe to the United States. In Figures 5.1 and 5.2 we see that both nominal and real investment in Europe has stagnated, or in fact, is expected to decline slightly in real terms, as per 2005 estimates. This chart confirms our expectations, based on what we saw earlier about the shifting of the R&D investments from Europe to the U.S., because of Europe’s more restrictive requirements.

The picture is almost similar to Europe, in the case of Japan, as can be seen from Figures 6.1 and 6.2. In fact, in the case of Japan there is a noticeable decline in R&D investments, both in nominal and real terms beyond the year 2000, with a slight reversal in the year 2002. This again supports the premise mentioned earlier of the continuous shifting of R&D investments to the United States from other global R&D centers, because of a better investment climate in the U.S. with less restrictive price control mechanisms. In spite of this, Japan still remains one of the world’s major new drug producers.
Figure 5.1 Nominal R&D spending – Europe

Figure 5.2 Real R&D spending – Europe
Figure 6.1 Nominal R&D spending – Japan

Figure 6.2 Real R&D spending – Japan
Although this thesis is deliberately excluding the government or quasi-government investments in R&D, it might be interesting to make a passing mention, just for comparison’s sake as to the quantum of government involvement and investments in R&D. Table 2 provides a snapshot on the NIH budget and PhRMA member organizations’ R&D expenditures in nominal U.S. dollars. Figure 7 is a graphical representation of the trends of R&D spending (as shown in related Table 2).

<table>
<thead>
<tr>
<th>Year</th>
<th>Total NIH Budget</th>
<th>PhRMA Member R&amp;D Expenditures</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>11.3</td>
<td>15.2</td>
</tr>
<tr>
<td>2000</td>
<td>17.8</td>
<td>26.0</td>
</tr>
<tr>
<td>2001</td>
<td>20.5</td>
<td>29.8</td>
</tr>
<tr>
<td>2002</td>
<td>23.7</td>
<td>31.0</td>
</tr>
<tr>
<td>2003</td>
<td>27.0</td>
<td>34.5</td>
</tr>
<tr>
<td>2004</td>
<td>28.0</td>
<td>37.0</td>
</tr>
<tr>
<td>2005**</td>
<td>28.6</td>
<td>39.4</td>
</tr>
</tbody>
</table>

**estimated
Figure 7 PhRMA R&D Expenditure and NIH Budget trends: 1995-2005
Figure 7 gives us a perspective of the private R&D expenditures in relation to government and quasi-government budgetary involvement in pharmaceutical R&D for the period 1995-2005** (**2005 figures are estimated). This clearly shows that in spite of the existing patent laws, the private sectors involvement in R&D has been significantly higher, when compared to the government sector. This is an encouraging sign, and extending patent protection may actually give the additional incentive to the industry to invest more heavily in R&D.

Studying this pattern in R&D investment, both in nominal and real terms, and correlating that with the global trends of the AIDS epidemic, 2008 (Appendix 1.2), what stands out in a fairly stark fashion, is that the pharmaceutical industry has not been able to deliver on newer drugs and anti-retroviral therapies so far. In spite of a piecemeal solution, by and large the prohibitive costs of available therapy have made even these drugs to both the population directly, or even for government purchases. One of the reasons that even governments have limited access to these therapies is that most of the sub-Saharan Africa (Appendix 5) where HIV/AIDS is of endemic proportions is financially unable to bear the cost of these therapies. As Appendix 1.2 shows, even on a global context, the AIDS epidemic has spread in the period 1990 – 2008, even though there appears to be a slight tapering in the years 2005-2008. Looking at this a little more in details shows that increasing awareness, educational efforts, and preventive measures probably contributed to this effect, rather than availability of newer or better drugs.
Figure 8 gives us a picture of the drug launches in the period 2000 – 2005 by eighty-nine pharma companies in the Lehman universe\(^{10}\). As can be seen clearly, there is a declining trend of numbers in the new drug launches over the time period of study. Of course, here we are taking into account the launches globally, which accounts for pharmaceutical companies from different countries of the world, which also includes the U.S. companies.

\[\text{Drug Launches}\]

\[\begin{array}{c}
\text{Number of drugs} \\
\text{2000} \quad \text{2001} \quad \text{2002} \quad \text{2003} \quad \text{2004} \quad \text{2005} \\
\text{All drugs}
\end{array}\]

\(^{10}\) In its 2002 edition of *PharmaPipelines*, Lehman Brothers projects the launch schedule (2000-2005) for the companies in its universe, providing an overview of the overall industry launches probability adjusted for current phase of development and their expected commercial potential. For each company, Lehman records a launch when a new molecular entity is launched in its first major market. When more than one company launches a drug as a sole marketer, co-marketer or in a joint venture, the product will be recorded for both companies. For future years, the launch data is probability-adjusted, something that is reflected in fractions of numbers of drugs apparently coming to the market. (PAREXEL’s Pharmaceutical R&D Statistical Sourcebook 2002)
Figures 9.1 – 9.7 show the worldwide active R&D projects in development by stage, i.e., from the pre-clinical stage to the launched phase, for the period 1998 – 2002\textsuperscript{11}. In all these set of graphs, the vertical axis denotes the number of active R&D projects and the horizontal axis shows the years for the period 1998 to 2002.

\textsuperscript{11} Source: Pharmaprojects (PAREXEL’s Pharmaceutical R&D Statistical Sourcebook 2002)
It is worth noting that, though there is upward trend in the number of active R&D projects in each of the pre-clinical, phase 1, phase 2, and phase 3 stages, the trend changes dramatically in the pre-registered and registered stages. When it comes to actual launching of a drug in the market, the trend is downward, implying sufficient number of drugs from the active R&D projects are not actually making it to the market. This is also corroborated by the earlier trend we saw in Figure 8, in terms of drug launch trends. A possible cause could be the costs and increased regulatory requirements to get to the launch phase, in addition to the inadequate incentives in the present patent system.
Against the backdrop of the above global information and trends, let us take a look at the areas of new U.S. clinical trial starts for drugs as measured by the Investigational New Drug (IND) submissions to respective FDA Review Divisions for the period 1997 – 2001. Since we are focusing on the newer drugs in the context of treatment of HIV/AIDS, let us specifically focus on three categories of related drugs: anti-infectives, anti-virals and immunologic drugs. Figure 10 shows us the trends of IND submissions for each of these categories.

![Figure 10 Total IND submissions](image)

Each of these categories of drugs which are critical for the treatment of HIV/AIDS, shows overall declining trends. The anti-viral drugs have a slightly reversed trend between 2000 – 2001, but the 2001 number till remains below the 1997 level. This again shows that there are just not enough drugs coming into the market to tackle the growing threat of HIV/AIDS. The lack of newer drugs and availability of treatment regimens for
already infected populace is having a detrimental impact in the ability to control the spread of HIV/AIDS, in most parts of the world, especially where the condition has already reached endemic proportions, like sub-Saharan Africa (Appendix 5). Again a possible reason could be the lack of enough incentives in terms of longer term patent protection which is driving this, in addition to other factors.

According to Pharmaprojects, a database that tracks pharmaceutical R&D worldwide, after peaking in 1997, when there were 288 new drugs in active development, antiretroviral HIV R&D has declined in the subsequent years (1998 – 2000). By mid-2000, only 188 retroviral drugs were in development, a decline of 35% in three years. On the other hand after hitting a trough in 1997, a number of AIDS vaccine products under development have been on a modest, and steady increase. A possible cause – it is difficult to imitate vaccines or alter process to produce ‘generic’ vaccines. So, in this case, the pharmaceutical and bio-pharmaceutical companies have a greater incentive to invest in this area of R&D. This is because even after expiration of patent protection periods, there is unlikely to be a deluge of generic vaccines hitting the market. In effect, this lack of major competition in this sector acts, by default, like a longer term patent protection. This reinforces the thinking that patents in perpetuity can give the incentive to industry to invest more in R&D.
CHAPTER V
DISCUSSIONS & CONCLUSIONS

One of the main objectives of this study was to analyze available empirical data to find out if there is any likely correlation between longer, if not perpetual, patent durations for pharmaceuticals with availability of cheaper life saving drugs in a specific instance of the HIV/AIDS conditions. Consumers getting better and less costly products should be the aim of any policy which aims to increase human welfare. The Hatch-Waxman Act of 1984 was intended to help lower-cost generics get into the market. That satisfies only one of the requirements, viz., getting lower cost drugs into the market. It does not address the issue of getting better products into the market. This is because generics have the benefit of lower cost, but since they are just ‘copycat’ products, they do not meet the criteria of a better product in terms of better therapeutics. Moreover, there are considerable differences of opinion as to the efficacy and bio-equivalence of generics, as compared to branded products in the medical fraternity. Perceptions exist in the physicians mind, based on clinical experience and observation, that generics can be less effective than branded products to the extent of up to thirty percent. Though conclusive evidence may not be available, it still affects diagnostics and treatment, and doctors are many a time forced to accept generic substitutions, purely based on insurance restrictions, or demands from patients for lower cost drugs. This study tries to show the connection between
longer pharmaceutical patents leading to increased welfare through lowering of vital drug prices, without compromising the quality aspect of better products.

The process and the thinking behind this are fairly simple. The study looks at a scenario where the government steps back and lets the ‘Invisible hand’ of the market operate. The role of the government is limited to ensuring ‘property rights’, i.e., in this case patent rights, so that the government like other instances of protecting property rights, ensures that ‘patent rights’ are protected from infringement by the law of the land. This requirement is, of course, going to be universal, and has to be ensured by bodies such as the World Trade Organization, or any such newly created entity. This in turn provides the worldwide pharmaceutical industry with the necessary incentives to invest in basic research, thus leading to discoveries of newer drugs. The successful drugs which ultimately become available in the market will not have to recoup the R&D costs in a specific and limited time frame of patent duration, before the generics hit the market. Under this scenario, and keeping in mind the concept of the ‘Product Life Cycle’, pharmaceutical firms will be able to spread out the R&D costs over a considerable longer period, which in turn will allow for drug prices to be more affordable. Of course, there is a need to extend this study to other pathological conditions, and the evolving and available therapies for such conditions, to decide more conclusively on the welfare implications of perpetual patents for pharmaceuticals.
REFERENCES


APPENDICES
APPENDIX A

GLOBAL ESTIMATES FOR ADULTS AND CHILDREN, 2008

Figure 11. Global estimates for adults and children, 2008

Source: UNAIDS/WHO (2009 AIDS epidemic update – December 2009). The ranges around the estimates in this table define the boundaries within which the actual numbers lie, based on the best available information.
APPENDIX B

GLOBAL SUMMARY OF THE AIDS EPIDEMIC, 2008

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>33.4 million [31.1 – 35.8 million]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of people living with HIV in 2008</td>
<td>Adults</td>
<td>31.3 million [29.2 – 33.7 million]</td>
</tr>
<tr>
<td></td>
<td>Women</td>
<td>15.7 million [14.2 – 17.2 million]</td>
</tr>
<tr>
<td></td>
<td>Children</td>
<td>2.1 million [1.2 – 2.9 million]</td>
</tr>
</tbody>
</table>

| People newly infected with HIV in 2008 | Total      | 2.7 million [2.4 – 3.0 million]   |
|                                        | Adults     | 2.3 million [2.0 – 2.5 million]   |
|                                        | Children   | 430,000 [240,000 – 610,000]       |

| AIDS-related deaths in 2008            | Total      | 2.0 million [1.7 – 2.4 million]   |
|                                        | Adults     | 1.7 million [1.4 – 2.1 million]   |
|                                        | Children   | 280,000 [160,000 – 410,000]       |

Source: UNAIDS/WHO (2009 AIDS epidemic update – December 2009). The ranges around the estimates in this table define the boundaries within which the actual numbers lie, based on the best available information.
APPENDIX C

ADULTS AND CHILDREN ESTIMATED TO BE LIVING WITH HIV, 2008

APPENDIX D

GLOBAL TRENDS OF THE AIDS EPIDEMIC, 2008

(graphical representation)

Figure 14. Global trends of the AIDS epidemic, 2008

Source: UNAIDS/WHO (2009 AIDS epidemic update) – graph from AVERT [AVERTing HIV and AIDS]
APPENDIX E

ESTIMATED NUMBER OF AIDS-RELATED DEATHS WITH AND WITHOUT ANTIRETEOVIRAL THERAPY, GLOBALLY, 1996-2008

Figure 15. Estimated number of AIDS-related deaths with and without antiretroviral therapy, globally, 1996–2008

APPENDIX F
GLOBAL ESTIMATES 1990-2008

Global estimates 1990–2008

![Graphs showing global estimates 1990-2008](chart)

Figure 16. Global estimates 1990-2008

APPENDIX G

NORTH AMERICA AND WESTERN AND CENTRAL EUROPE ESTIMATES 1990-2008

North America and Western and Central Europe estimates 1990–2008

Figure 17. North America and Western and Central Europe estimates 1990-2008

APPENDIX H

ESTIMATE OF THE ANNUAL NUMBER OF INFANT INFECTIONS AVERTED THROUGH THE PROVISION OF ANTIRETROVIRAL PROPHYLAXIS TO HIV-POSITIVE PREGNANT WOMEN, GLOBALLY, 1996-2008

Estimate of the annual number of infant infections averted through the provision of antiretroviral prophylaxis to HIV-positive pregnant women, globally, 1996–2008

Figure 18. Estimate of the annual number of infant infections averted through the provision of antiretroviral prophylaxis to HIV-positive pregnant women, globally, 1996-2008

APPENDIX I

THE FOLLOWING IS A LIST OF THE TWELVE LARGEST PHARMACEUTICAL COMPANIES RANKED BY REVENUE AS OF 2008 IN THE FORTUNE GLOBAL 500

Table 3. List of twelve largest pharmaceutical companies by revenue in 2008

<table>
<thead>
<tr>
<th>Rank</th>
<th>Company</th>
<th>Country</th>
<th>Total Revenues 2008 (USD billions)</th>
<th>Net income/loss 2008 (USD billions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pfizer (with Wyeth)</td>
<td>U.S.</td>
<td>70.7</td>
<td>14.1</td>
</tr>
<tr>
<td>2</td>
<td>Johnson &amp; Johnson</td>
<td>U.S.</td>
<td>63.8</td>
<td>10.6</td>
</tr>
<tr>
<td>3</td>
<td>Bayer</td>
<td>Germany</td>
<td>48.2</td>
<td>6.4</td>
</tr>
<tr>
<td>4</td>
<td>Hoffmann–La Roche</td>
<td>Switzerland</td>
<td>44.0</td>
<td>8.1</td>
</tr>
<tr>
<td>5</td>
<td>Novartis</td>
<td>Switzerland</td>
<td>41.5</td>
<td>11.9</td>
</tr>
<tr>
<td>6</td>
<td>GlaxoSmithKline</td>
<td>UK</td>
<td>40.4</td>
<td>10.4</td>
</tr>
<tr>
<td>7</td>
<td>Sanofi-Aventis</td>
<td>France</td>
<td>40.3</td>
<td>7.2</td>
</tr>
<tr>
<td>8</td>
<td>AstraZeneca</td>
<td>UK/Sweden</td>
<td>31.6</td>
<td>6.0</td>
</tr>
<tr>
<td>9</td>
<td>Abbott Laboratories</td>
<td>U.S.</td>
<td>29.5</td>
<td>4.9</td>
</tr>
<tr>
<td>10</td>
<td>Merck &amp; Co.</td>
<td>U.S.</td>
<td>23.9</td>
<td>7.8</td>
</tr>
<tr>
<td>11</td>
<td>Bristol-Myers Squibb</td>
<td>U.S.</td>
<td>20.0</td>
<td>2.2</td>
</tr>
<tr>
<td>12</td>
<td>Eli Lilly and Company</td>
<td>U.S.</td>
<td>18.6</td>
<td>3.0</td>
</tr>
</tbody>
</table>
APPENDIX J

GLOBAL PHARMA R&D EXPENDITURE – MORE RECENT TRENDS

Figure 19. Global pharma R&D expenditure – more recent trends

The Center for Medicines Research International (CMR International) found that global pharmaceutical R&D expenditure exceeded US$56 billion in 2004. This total expenditure on all R&D activities (e.g. salaries, other personnel-related costs, costs related to consumable material and supplies, and appropriate share of overhead to cover administration, depreciation, space charges, rent, etc.) related to ethical pharmaceuticals, which include chemical entities, biological products, biotech entities, gene therapy products, or in vivo diagnostics. This expenditure includes capital R&D expenditure as
well as expenditure on R&D conducted by means of grants or contracts to other companies or institutions and proportional costs for joint ventures.

The estimates of annual global R&D spending are based on data supplied directly to CMR international by up to 40 leading pharmaceutical companies in conjunction with data from a number of national pharmaceutical trade associations. Unlike many other published estimates of global R&D expenditure, effort is made to ensure that only expenditure related to ethical pharmaceuticals is captured.
## APPENDIX K

### 2007-2008 SUB-SAHARIAN AIDS SCENARIO, POPULATION WISE

**Table 4. 2007-2008 sub-Saharan AIDS scenario, population wise**

<table>
<thead>
<tr>
<th>Country</th>
<th>People living with HIV/AIDS</th>
<th>Adult (15-49) rate %</th>
<th>Women with HIV/AIDS</th>
<th>Children with HIV/AIDS</th>
<th>AIDS deaths</th>
<th>Orphans due to AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angola</td>
<td>190,000</td>
<td>2.1</td>
<td>110,000</td>
<td>17,000</td>
<td>11,000</td>
<td>50,000</td>
</tr>
<tr>
<td>Benin</td>
<td>64,000</td>
<td>1.2</td>
<td>37,000</td>
<td>5,400</td>
<td>3,300</td>
<td>29,000</td>
</tr>
<tr>
<td>Botswana</td>
<td>300,000</td>
<td>23.9</td>
<td>170,000</td>
<td>15,000</td>
<td>11,000</td>
<td>95,000</td>
</tr>
<tr>
<td>Burkina Faso</td>
<td>130,000</td>
<td>1.6</td>
<td>61,000</td>
<td>10,000</td>
<td>9,200</td>
<td>100,000</td>
</tr>
<tr>
<td>Burundi</td>
<td>110,000</td>
<td>2</td>
<td>53,000</td>
<td>15,000</td>
<td>11,000</td>
<td>120,000</td>
</tr>
<tr>
<td>Cameroon</td>
<td>540,000</td>
<td>5.1</td>
<td>300,000</td>
<td>45,000</td>
<td>39,000</td>
<td>300,000</td>
</tr>
<tr>
<td>Central African Republic</td>
<td>160,000</td>
<td>6.3</td>
<td>91,000</td>
<td>14,000</td>
<td>11,000</td>
<td>72,000</td>
</tr>
<tr>
<td>Chad</td>
<td>200,000</td>
<td>3.5</td>
<td>110,000</td>
<td>19,000</td>
<td>14,000</td>
<td>85,000</td>
</tr>
<tr>
<td>Comoros</td>
<td>&lt;200</td>
<td>&lt;0.1</td>
<td>&lt;100</td>
<td>&lt;100</td>
<td>&lt;100</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Congo</td>
<td>120,000</td>
<td>3.5</td>
<td>43,000</td>
<td>6,600</td>
<td>6,400</td>
<td>69,000</td>
</tr>
<tr>
<td>Côte d’Ivoire</td>
<td>480,000</td>
<td>3.9</td>
<td>250,000</td>
<td>52,000</td>
<td>38,000</td>
<td>420,000</td>
</tr>
<tr>
<td>Dem. Republic of Congo</td>
<td>400,000-</td>
<td>1.2-</td>
<td>210,000-</td>
<td>37,000-</td>
<td>24,000-</td>
<td>270,000-</td>
</tr>
<tr>
<td>Djibouti</td>
<td>16,000</td>
<td>3.1</td>
<td>8,700</td>
<td>1,100</td>
<td>1,100</td>
<td>5,200</td>
</tr>
<tr>
<td>Equatorial Guinea</td>
<td>11,000</td>
<td>3.4</td>
<td>5,900</td>
<td>&lt;1,000</td>
<td>&lt;1,000</td>
<td>4,800</td>
</tr>
<tr>
<td>Eritrea</td>
<td>38,000</td>
<td>1.3</td>
<td>21,000</td>
<td>3,100</td>
<td>2,600</td>
<td>18,000</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>980,000</td>
<td>2.1</td>
<td>530,000</td>
<td>92,000</td>
<td>67,000</td>
<td>650,000</td>
</tr>
<tr>
<td>Gabon</td>
<td>49,000</td>
<td>5.9</td>
<td>27,000</td>
<td>2,300</td>
<td>2,300</td>
<td>18,000</td>
</tr>
<tr>
<td>Gambia</td>
<td>8,200</td>
<td>0.9</td>
<td>4,500</td>
<td>&lt;1,000</td>
<td>&lt;1,000</td>
<td>2,700</td>
</tr>
<tr>
<td>Ghana</td>
<td>260,000</td>
<td>1.9</td>
<td>150,000</td>
<td>17,000</td>
<td>21,000</td>
<td>160,000</td>
</tr>
<tr>
<td>Guinea</td>
<td>87,000</td>
<td>1.6</td>
<td>48,000</td>
<td>6,300</td>
<td>4,500</td>
<td>25,000</td>
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<tr>
<td>Guinea-Bissau</td>
<td>16,000</td>
<td>1.8</td>
<td>8,700</td>
<td>1,500</td>
<td>1,100</td>
<td>6,200</td>
</tr>
<tr>
<td>Kenya</td>
<td>1,500,000-</td>
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APPENDIX L

DATA SOURCES

- PAREXEL’s Pharmaceutical R&D Statistical Sourcebook 2002/2003
- WHO ICD-10 (International Classification of Diseases), mortality data for the tenth revision
- Food and Drug Administration (United States)