# THE INVENTION OF AN INVESTMENT INCENTIVE FOR PHARMACEUTICAL INNOVATION

Thesis submitted in partial fulfillment of the requirements
for the Degree of Doctor of Philosophy

**by**

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**AUTHORSHIP DECLARATION**

I hereby certify that this thesis is the result of my own work except where otherwise indicated and due acknowledgement is given.

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Shamnad Basheer 3 October 2011

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## ABSTRACT

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Pharmaceutical drugs are often hailed as the poster child for the proposition that patents foster accelerated rates of innovation. This sentiment stems, in large part, from the significantly high research and development (R&D) costs endemic to the pharmaceutical sector. I argue that if the role of the patent regime is one of fostering higher amounts of investment in the R&D process, it is better served by a direct investment protection regime, where the protection does not depend upon whether or not the underlying idea behind the drug is "new" and "inventive", the two central tenets of patent law. Rather, any drug that successfully makes it past the regulatory filter ought to be entitled to protection, since its discovery and development entail significant investment and risk.

Owing to the inadequacy of the current patent regime in appropriately protecting intensive pharmaceutical R&D investments from free-riders, I propose a comprehensive investment protection regime that protects all the investment costs

incurred during the drug discovery and development process. Though similar to existing data protection regimes in some respects, it differs in others. Firstly, it enables a recovery of all R&D costs, and not only costs associated with clinical trials. Secondly, unlike patents and data exclusivity which offer uniform periods of protection, it rewards investments in a proportionate manner, wherein drug originators are entitled to protection against free-riders only until such time as they recoup their specific investments and earn a rate of return on investment that is dependent on the health value of the drug.

Given that a pure market exclusivity based investment protection regime is likely to foster excessive pricing and subject the market to the dictates of a single firm, I advocate a compensatory liability model based on a novel cost sharing methodology, where follow-on entrants are free to manufacture the drug, but must pay a reasonable amount of compensation to the originator.

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This thesis has strong roots in the desire of a truly exceptional lady to see a “Dr.” appended to her son’s name. As with all other middle class mothers from Kerala, an Indian state that arrogates to itself the epithet, “God’s own country”, she meant a “doctor” from the medical fraternity. Unfortunately, given that the son could not bring himself to appreciate the various nuances in the reproductive cycle of an Amoeba during his school lessons, the medical profession proved to be an elusive dream.

Many years later, a post-graduate stint at Oxford rekindled the dream, albeit in another form. The son hopes that his mother would, in the spirit of Lord Denning’s philosophy, eschew a strict literal construction in favour of a spirited one and settle for a DPhil induced “Dr”. Particularly since the subject matter of the DPhil thesis relates to medicine.

But for my mothers’ wish, I might not have had the patience to subject myself to the rather arduous DPhil process. So I begin this work of love by recording my appreciation for the wonderful inspiration provided by her. If I can live up to a tenth of the values that she stood for, I will consider my existence justified on this earth. I dedicate this work to her memory.

There are several others who played instrumental roles in seeing this DPhil thesis to its completion. I must seek your indulgence as I take you through this incredibly diverse list of people and institutions that destiny brought together to ensure the fulfilment of a mothers' wish:

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14. And last, but not least, my heartfelt gratitude to the wonderful Arunachala, a mountain in the shady groves of which I penned most of the ideas that underlie this thesis.

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## LIST OF ABBREVIATIONS

| | |
|---|---|
| AMC | ADVANCE MARKET COMMITMENT |
| ANDA | ABBREVIATED NEW DRUG APPLICATION |
| APC | ADVANCED PURCHASE CONTRACT |
| CML | CHRONIC MYLOID LEUKEMIA |
| CTA | CLINICAL TRIAL AUTHORISATION |
| DALY | DISABILITY ADJUSTED LIFE YEARS |
| DNA | DEOXYRIBONUCLEIC ACID |
| EEC | EUROPEAN ECONOMIC COMMUNITY |
| EFPIA | EUROPEAN FEDERATION OF PHARMACEUTICAL INDUSTRIES AND ASSOCIATIONS |
| EMEA | EUROPEAN MEDICINES AGENCY |
| EPO | EUROPEAN PATENT OFFICE |
| EU | EUROPEAN UNION |
| FDA | FOOD AND DRUG ADMINISTRATION |
| FIFRA | FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT |
| FOSS | FREE AND OPEN SOURCE SOFTWARE |
| FTA | FREE TRADE AGREEMENT |
| GBD | GLOBAL BURDEN OF DISEASE |
| GPL | GENERAL PUBLIC LICENCE |
| HALYS | HEALTH ADJUSTED LIFE YEARS |
| hGH | HUMAN GROWTH HORMONE |

| | |
|---|---|
| HIF | HEALTH IMPACT FUND |
| HRQL | HEALTH RELATED QUALITY OF LIFE |
| HUI | HUMAN UTILITIES INDEX |
| ICTSD | INTERNATIONAL CENTRE FOR TRADE AND SUSTAINABLE DEVELOPMENT |
| IND | INVESTIGATIONAL NEW DRUG |
| INDA | INVESTIGATIONAL NEW DRUG APPLICATION |
| MED | MALE ERECTILE DYSFUNCTION |
| NAFTA | NORTH AMERICAN FREE TRADE AGREEMENT |
| NCE | NEW CHEMICAL ENTITY |
| NDA | NEW DRUG APPLICATION |
| NHS | NATIONAL HEALTH SERVICES |
| NICE | NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE |
| NIH | NATIONAL INSTITUTE OF HEALTH |
| NME | NEW MOLECULAR ENTITY |
| OSDD | OPEN SOURCE DRUG DISCOVERY |
| OTA | OFFICE OF TECHNOLOGY ASSESSMENT |
| PDE VA | PHOSPHODIESTERASE VA |
| PhRMA | PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA |
| QALY | QUALITY ADJUSTED LIFE YEARS |
| r-hGH | RECOMBINANT HUMAN GROWTH HORMONE |
| RNA | RIBONUCLEIC ACID |
| SADC | SOUTHERN AFRICAN DEVELOPMENT COMMUNITY |

| | |
|---|---|
| SPC | SUPPLEMENTAL PROTECTION CERTIFICATES |
| TBR | TRADE BARRIERS REGULATION |
| W.M.A. | WORLD MEDICAL ASSOCIATION |
| WDE | WHOLE DRUG EQUIVALENTS |
| YLD | YEARS LIVED IN DISABILITY |
| YLL | YEARS OF LIFE LOST |

## TABLE OF CASES

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## INTRODUCTION

In this thesis, I seek to investigate the adequacy of current legal incentives for fostering investment in pharmaceutical R&D. Finding that the current incentive regimes in the form of patents and data exclusivity suffer a number of drawbacks, I propose a more optimal investment protection regime.

As far back as 1976, a commentator noted that: "[w]ithout patents, the return from investment in pharmaceutical research and development would fall to zero, and private companies would no longer engage in research and development."[1]

This sentiment continues unabated till this day, and even those that question the general nexus between patents and innovation admit that the pharmaceutical industry is an exception.[2] Illustratively, Bessen and Meurer, two of the most vocal critics of the patent system, note that, "(i)n some industries, such as pharmaceuticals, patents provide strong positive incentives to invest in innovation. But in many other industries, perhaps most, patents fail to perform like property

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[1] *See* DAVID SCHWARTZMAN, INNOVATION IN THE PHARMACEUTICAL INDUSTRY (1976).

[2] *See* Amy Kapczynski et al., *Addressing Global Health Inequities: An Open Licensing Approach for University Innovations*, 20 BERKELEY TECH. L. J. 1031, 1044–45 (2005) ("Many who accept these premises [that strong patents reduce innovation and welfare] nonetheless consider the pharmaceutical sector an exception."); *see also* Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability* 87 TEX. L. REV. 503 (2009). ("[P]harmaceutical innovation is thought to be the patent system's greatest success story."); *see also* WILLIAM M. LANDES & RICHARD A. POSNER, THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW 316 (2003) ("[T]he strongest case for patents in something like their present form is said to be found in a subset of the drug industry.").

and they may actually discourage innovation."[3]

While this statement may generally hold true, I argue that the patent regime is sub-optimal when it comes to protecting investments. If the role of the patent system is conceptualised as one of fostering higher levels of investment into the pharmaceutical R&D process, this function is more optimally achieved through a direct investment protection regime that does not depend on compliance with traditional patentability criteria such as "novelty" and "inventive step".[4]

In other words, a regime that grants comprehensive market exclusivity to new drugs against free riders until such time as the investment in the discovery and development of that drug is recouped is preferable to a patent regime. I elaborate upon such a regime in the ensuing chapters. This regime draws in some ways from existing regulatory data exclusivity regimes, which protect investment costs incurred in the course of generating regulatory data through clinical trials i.e.

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[3] *See* James Bessen & Michael J. Meurer, *Of Patents and Property*, 31(4) REGULATION 18, 19 (2008-09); *see also* JAMES BESSEN & MICHAEL J. MEURER, PATENT FAILURE: HOW JUDGES, LAWYERS, AND BUREAUCRATS PUT INNOVATORS AT RISK (2008); *see also* J. P. Walsh et al., *Effects of Research Tool Patenting and Licensing on Biomedical Innovation, in* PATENTS IN THE KNOWLEDGE BASED ECONOMY 285 (Wesley M. Cohen & Stephen Merrill eds., 2003). For a discussion on how patents are likely to increase investments and thereby the rate of innovative output in industries such as pharmaceuticals, see Bronwyn H. Hall, *Patents and Policy*, 23(4) OXFORD REV. ECON. POL. 575 (2007) (citing E. Mansfield, *Patents and Innovation: An Empirical Study*, 32(2) MANAGEMENT SCIENCE 173, 173-181 (1986)).

[4] The novelty and non-obviousness principles are designed to work together to ensure that the patent monopoly is available only for genuinely new inventions. The novelty standard asks whether the invention has been previously described or practiced, and actually looks at previous references and practices; it thus determines whether the invention is within the existing state of the art. The non-obviousness principle then asks whether the invention is an adequate distance beyond or above that state of the art; it clearly and unavoidably, therefore, involves a judgment call. John Barton, *Non-Obviousness*, 43 IDEA 475 (2003).

"safety" and "efficacy" data, which are required to be submitted to a drug regulatory authority to procure marketing approval.[5] This regulatory data generation accounts for a major part of drug discovery and development costs.[6] Countries such as the United States of America (hereinafter "U.S.") and the European Union countries (hereinafter "EU") protect the investments underlying this data generation by granting a fixed term of market exclusivity, during which time no competitor can rely on the data submitted by the drug originator.

However, while a data exclusivity regime could be considered an explicit investment protection tool and is therefore more optimal than a patent regime on this count, it suffers from certain shortcomings. Firstly, it provides for a uniform period of protection, without regard to the specific investment made per drug or the health impact of a drug. Secondly, it only accounts for the costs incurred during the clinical trial process and excludes significant investments made at the drug discovery and pre-clinical stages.

I advocate a comprehensive, yet calibrated investment protection regime that grants protection from free-riders who threaten to disrupt the market share of the drug originator with a largely "similar" drug molecule, until such time as the

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[5] *See generally* Gerald Mossinghoff, *Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process*, 54 FOOD & DRUG L. J. 187 (1999).

[6] *See* Joseph A. DiMasi et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22(2) JOURNAL OF HEALTH ECONOMICS 151, 165 (2003).

investments are recouped along with a rate of return on the investment commensurate with the health impact of the drug.

Owing to the potential dangers of an exclusive market controlled by a single firm and the threat of excessive pricing and reduced access to medicines, I advocate a compensatory liability regime, which eschews any kind of market exclusivity, leaving the drug originator with the mere right to claim reasonable compensation from follow-on entrants. I propose a new framework for assessing fair compensation in this regard.

Once it is appreciated that the function of investment protection is better addressed through a separate stand-alone regime, the pressure on patents to fulfil a role for which it is not originally designed, abates. This point is an important one to appreciate, as the conflation between patent protection and investment protection has caused many to argue for a dilution of the patentability threshold.[7]

Lastly, this thesis argues that the introduction of a comprehensive investment protection regime dispenses with the need to have a data exclusivity regime.

### A. Contribution

[7] *See infra* text accompanying notes 214-216.

The key contribution of this thesis is in demonstrating that a comprehensive investment protection regime is far more optimal than the current patent and data exclusivity regimes in protecting the significant investments in drug discovery and development.

Although scholars have highlighted the limitations of the patent regime in supporting pharmaceutical innovation in an optimal manner, none have proposed a comprehensive investment protection regime, as that proposed in this thesis. Even those that focus on investment protection advocate the use of the data exclusivity regime. This thesis demonstrates the limitations of the data exclusivity regime, the most obvious of which is that the protection is tied to the submission of regulatory data and covers only costs relating to clinical trials. Further, it is a uniform period of protection without regard to the specific amount of investment or the health impact of the drug.

Lastly, the thesis proposes an inbuilt compulsory licensing mechanism or a broader compensatory liability model in order to provide against the potential abuse of the granted monopoly by a drug originator, who excessively prices the drug or is not able to supply the market adequately. It advocates that follow-on innovators be permitted to enter the market upon the payment of reasonable compensation to the drug originator. It proposes a novel methodology of computing compensation, whereby a reasonable amount, which balances the interests of both the drug originator and the follow on manufacturer has to be paid.

The compensation methodology takes into account the global nature of pharmaceutical innovation and the international market for drugs.

## B. Chapterisation

The thesis proceeds in Chapters as below:

Chapter I of the thesis discusses the framework for pharmaceutical R&D in order to help appreciate the intensive investments and risks underlying pharmaceutical innovation.

Chapter II explores the role of patents in pharmaceutical innovation and points out why the regime is sub-optimal from the point of view of protecting investments.

Chapter III discusses the data exclusivity regime (as prevalent in the U.S. and EU) and its nexus with pharmaceutical innovation.

Chapter IV outlines a comprehensive "investment protection" regime, under which drug originators are granted market exclusivity for a certain number of years after the drug has been approved. This period of protection is not a uniform one, but is based on the time taken by drug originators to recover the costs incurred in relation to each drug, as also an appropriate rate of return on investment based on

the "health impact" of the drug, measured through existing metrics such as QALY and DALY.[8] Such a calibrated protection regime is more optimal from a policy perspective, as it avoids over-compensating or under-compensating drug originators. Most importantly, it helps prevent the proliferation of "me too" drugs[9] through a process commonly referred to as ever-greening.[10]

The Chapter subsequently proposes an inbuilt compulsory licensing/compensatory liability regime, where the drug originator is not conferred with any market exclusivity. Rather, follow-on generic competitors may enter the market upon the payment of equitable remuneration. It proposes a novel compensatory methodology, taking into account the costs of drug discovery and development and the relative market shares of the originator and the follow-on generic entrant(s).

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[8] *See infra* text accompanying notes 329-373.

[9] *Compare* Haiden A. Huskamp, *Prices, Profits and Innovation: Examining Criticisms of the Value of New Psychotropic Drugs*, 25(3) HEALTH AFF 635 (2006) ("The first brand drug using a particular therapeutic mechanism of action is called a 'breakthrough drug,' while brand drugs that use the same mechanism of action but enter after the breakthrough drug are called 'me-too drugs.'") *with* US CONGRESS OFFICE OF TECHNOLOGY ASSESSMENT, OTA-H-522, PHARMACEUTICAL R&D: COSTS, RISKS AND REWARDS, (1993) http://www.princeton.edu/~ota/disk1/1993/9336/9336.PDF (noting that, however, the distinction between pioneers and me-too's is described as "fuzzy," since not all me-too drugs may be imitative).

[10] "Ever-greening" is not a formal concept of patent law. It is best understood as a social idea used to refer to the myriad ways in which pharmaceutical patent owners utilise the law and related regulatory processes to extend their high rent-earning intellectual monopoly privileges, particularly over highly profitable (either in total sales volume or price per unit) 'blockbuster' drugs. For a discussion on this point, see T. A. Faunce & J. Lexchin, *'Linkage' pharmaceutical ever-greening in Canada and Australia available at* http://law.anu.edu.au/StaffUploads/236-Art%20ANZHP%20Linkage%20Evergreening.pdf;. *see also infra* notes 451-453 and accompanying text.

Chapter V assesses the issue of TRIPS compatibility of the compensatory liability model outlined in Chapter IV.

Chapter VI revisits the issue of patents and their role in pharmaceutical innovation. It notes that since the function of investment protection is better served through a separate regime, one need not dilute patentability thresholds in order to achieve this. This point is an important one to appreciate, as the conflation between patent protection and investment protection has caused many to argue for a lowering of the patentability threshold.[11]

The Chapter notes that in the absence of compelling empirical evidence, the issue of whether or not patents foster significantly accelerated innovation remains unresolved. However, much in line with the wisdom of Machlup and Penrose, I caution against dispensing with the regime altogether. I also note that TRIPS does not offer member states the luxury to do away with the patent regime. However, states are free to insist on rigorous thresholds for patent grants in order to prevent ever-greening and the proliferation of me-too drugs.

In so far as existing data exclusivity regimes are concerned, given that they are sub-optimal in terms of their uniformity and the fact that they attempt to only

[11] *See* Mossinghoff, *supra* note 5.

reward efforts during the clinical trial phase, I argue that they be dispensed with in favour of a comprehensive, yet calibrated investment protection regime.

The Chapter then goes on to investigate the issue of upstream third party incentives and concludes that there are a number of non-patent alternatives that could provide strong incentives for invention. It also proposes an additional incentive in the form of a limited right to an Investigational New Drug Application (hereinafter "INDA") applicant.

Chapter VII examines the issue of innovation policy from a global and developmental perspective. It notes that although developing countries may wish to eschew market exclusivity enhancing regimes in the interests of patients and public health, and also in the interests of enhancing local innovative capacity, the issue may be more complex when viewed from a global innovation perspective. Given that such a global computation (the optimal number of countries that need to institute protection regimes in order to support a viable world market for new drugs) is very complex and beyond the scope of the thesis, I note that in so far as a certain number of countries already have patents and data exclusivity regimes covering pharmaceutical innovation, the said countries could be persuaded to implement a more optimal investment protection regime, as that recommended in this thesis.

Chapter VIII discusses alternative incentives for pharmaceutical innovation such as prizes and advanced market commitments. It weighs them up against the proposed investment protection regime and finds that while these alternative incentives hold a lot of promise for incentivising drugs for neglected or developing country diseases, they may not be as optimal when it comes to developed country diseases.

The last part concludes the thesis by highlighting the key arguments and proposals advanced.

## C. Definitional Aspects

1. Though it has come to acquire a near canonical status, the term "innovation" lacks a precise definition.[12] The origins of the term can be traced back to the Latin noun, *innovatio*, derived from the verb, *innovare,* which means to introduce something new.[13] A report attempting to define innovation notes: [14]

> Innovation is a term that may have several meanings, that vary according to the context. The definition should incorporate the concept of an action of introducing a new product into the market, the "innovative" object newly

[12] *See* Jeffrey K. Aronson, *Something New Everyday: Defining Innovation and Innovativeness in Drug Therapy*, 31(1) J. AMBUL. CARE MANAGE. 65 (2008).

[13] *See id.*

[14] *Erice Statement on Drug Innovation*, 65(3) BRIT. J. CLIN. PHARMACOL. 440, 440 (2007).

> brought on to the market, and the potential positive effect on users.

The report then proposes a specific definition for pharmaceutical innovation as below-

> [A] completely or partially new active substance or biological entity or combinations of such entities acting against a disease, relieving symptoms or preventing a disease through pharmacological or molecular mechanisms, and developed and made available as a medicinal product that can improve the quality of patient management and outcomes.[15]

For the purpose of this thesis, I draw on this definition to define pharmaceutical innovation as the creation of any new drug or the discovery of any new indication or use for an existing drug, for which regulatory approval is required.[16]

2. The term "pharmaceutical drug" will be used to refer to conventional "small molecule" pharmaceutical drugs (hereinafter referred to as "conventional pharmaceutical drugs") and to the newer wave of bio-pharmaceuticals[17] or biologics.[18] However, given that the biologics sector is

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[15] *Id*.

[16] *See* Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 321(g)(1) (1938), which defines a "drug" as an 'article intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in man or other animals.' However, I limit my focus in this thesis to incentives for only one category of drugs, namely that of "developed" country drugs, which include conventional drugs based on small molecules and biologics. I also do not deal specifically with vaccines, diagnostics or with pharmaceutical processes.

[17] *See* Ronald A. Rader, *What Is a Biopharmaceutical?* BIOEXECUTIVE INT'L. 60, 60-61 (2005) *available at* http://www.bioexecutiveintl.com/content/articles/frame.asp?ck=true&issue=0305&article=11 (last visited Sept. 30, 2011) (Rader, after noting the multifarious definitions of the term

relatively nascent, the context in this thesis will be provided largely by specific examples from the conventional pharmaceutical industry.

3. The thesis deals primarily with incentives for fostering pharmaceutical innovation in jurisdictions such as the U.S. and the EU. The purpose behind this focus is two-fold. Firstly, most originator drugs have their primary markets in these countries, and more often than not, drugs are attributable to firms whose principal place of business are in these countries. Secondly, most of the literature surrounding pharmaceutical innovation and incentives, particularly in relation to patents and data exclusivity relate to these jurisdictions. However, where relevant, other countries are discussed in this thesis. Illustratively, it is noted that a compensatory liability model may be better suited for technologically proficient developing countries such as India.

4. A corollary of the above mentioned focus on developed country markets is that the proposed investment protection regime is better suited towards fostering cures for diseases endemic to such countries, which I refer to for

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"biopharmaceutical" offers the following definition: "a pharmaceutical product manufactured by biotechnology methods (involving live organisms)").

[18] Rader notes that whereas biologics "are large protein molecules derived from living cells and manufactured through DNA or RNA synthesis," conventional drugs "are small molecules derived from chemical synthesis," and additionally, conventional drugs "typically have well-defined structures." He further argues that by contrast, biologics 'tend to be a mixture of heterogeneous proteins and impurities, each of which may contribute to the product's biological activity, efficacy, and safety in ways that may be only partly understood, controlled and reproduced. *Id.* at 560.

the sake of convenience as "developed country" diseases. As elaborated upon in Chapter VII, this includes Type I diseases and some Type II diseases that have a significant financial footprint in the developed world. Given this limitation, the models proposed in this thesis are not likely to foster cure for diseases that are often referred to as "developing country" diseases (comprising of Type III diseases and Type II diseases which do not have a significant financial footprint in the developed world).

5. I use the term "drug originator" or "innovator" to refer to the firm that first acquires regulatory approval for a new drug or a new use for an existing drug. Similarly, I use the term "generic" and "follow-on" entrant/manufacturer interchangeably to refer to any additional drug applicant that wishes to enter the market with an active ingredient that is "similar" to that of the drug originator. The drug by the originator or innovator is referred to as the "pioneer" drug, and the drug by the generic or follow-on manufacturer is referred to as the "generic" drug.

6. As the majority of the drugs that are developed and marketed today have a significant infusion of private sector investment,[19] the solutions proposed in this thesis fall largely within the framework of market incentives for private firms. Nevertheless, I do contrast this approach with

[19] *See* Bhaven N. Sampat, *Academic Patents and Access to Medicines in Developing Countries*, 99(1) AM. J. PUB. HEALTH 9 (2009).

one that relies on public funding in Chapter VIII, which deals with alternative innovation incentives.

7. This thesis aims to work within the current framework of the Agreement on Trade-Related Aspects of Intellectual Property Rights (hereinafter "TRIPS") and proposes models that are likely to be TRIPS-compliant.

8. This thesis does not purport to deal with innovation policy as a whole; rather, it confines itself to one aspect of it, viz. that of providing incentives to invest in R&D by providing legal protection against free-riders until such time as costs of R&D and an appropriate rate of return on investment are recouped by the originator. Further, this thesis deals only with pharmaceutical innovation, a category of innovation that merits distinct attention for reasons below:[20]

   i) Significant R&D investments are required for new drugs,[21] when compared with other areas of technology such as software and

[20] *See* Rebecca S. Eisenberg, *The Role of The FDA in Innovation Policy*, 13 MICH. TELECOMM. TECH. L. REV. 345 (2007) (noting the broader political appeal enjoyed by health-related innovation). She argues:

> The reason that the budget of the National Institutes of Health (NIH) has grown, even as the budgets of other science agencies have languished, is that health-related innovation enjoys broader political appeal than other scientific pursuits. We value health, and we believe that high quality biomedical science will have public health payoffs.

[21] *See* Henry Grabowski, *Public Policy and Innovation: The Case of Pharmaceuticals*, 1 TECHNOVATION 157, 158 (1982).

electronics.[22] However, once the drug is approved, the cost of imitation is considerably lower than that incurred by the drug originator.

ii) Drugs are essential commodities, unlike other innovation goods such as electronics and software.[23] The lack of access to new drugs has a deleterious impact on public health and human rights.[24]

These definitional aspects will have to be borne in mind, as this thesis proposes to articulate a new legal regime for incentivising pharmaceutical innovation in the ensuing Chapters.

## D. Methodology

I have attempted to discard a purely formalistic, doctrinal approach in favour of a richer inter-disciplinary one, where I assess the views of economists, scientists and historians. It is my sincere belief that this rich inter-disciplinary weaving of materials makes for more convincing policy arguments and provides a firmer base

[22] The US Congress Budget Office states that pharmaceutical firms invest as much as five times more in research and development, relative to their sales, than the average US manufacturing firm. U.S. CONGRESS BUDGET OFFICE [hereinafter U.S. CBO], Pub. No. 2589, RESEARCH AND DEVELOPMENT IN THE PHARMACEUTICAL INDUSTRY, at 9-10, (2006), http://www.cbo.gov/ftpdocs/76xx/doc7615/10-02-DrugR-D.pdf.

[23] *See* Inge Kaul & Michael Faust, *Global Public Goods and Health: Taking the Agenda Forward*, 79(9) BULL. WORLD HEALTH ORG. (2001), *available at* http://www.scielosp.org/scielo.php?pid=S0042-96862001000900013&script=sci_arttext (last visited Jan. 16, 2011).

[24] *See* Bernard Munos, *Lessons from 60 years of Pharmaceutical Innovation*, 8 NATURE REVIEWS DRUG DISCOVERY 959, 967 (2009).

upon which to premise the legal regime that I advocate in this thesis. At the same time, I am aware of the shortcomings of inter-disciplinary scholarship, as well as the lawyer's tendency to cherry pick material favouring the argument being advanced.

Although my final proposal is an international regime that countries would have to implement domestically, most of the policy analysis draws on existing materials from the US and EU. The reason for this has been explained in the earlier section.

I conclude the Introduction with some notes on housekeeping. The mode of citation adopted is modelled on the Harvard Bluebook (for which prior permission has been procured from the University). Spellings have been standardised for ease of perusal and internal citations have been omitted in extended quotations. All internet references are valid as of Sept. 30, 2011.

## CH. I: DRUG DISCOVERY AND DEVELOPMENT: AN OVERVIEW

The drug discovery and development process is characterised by high risk and investment, as outlined below. I focus mainly on the US and EU regulatory frameworks.

### A. Stages of Drug Discovery and Development

The process for bringing a drug to the market can be classified into three broad stages: (i) the discovery phase; (ii) the pre-clinical phase; and (iii) the clinical trial phase.[25]

#### 1. Discovery Phase

Since the "discovery" phase is what effectively heralds the concrete search for a new drug, it will be used in this thesis as the starting point of the timeline for the purpose of computing the costs associated with drug discovery and development. At its very core, this stage involves the search for a "target," followed by that of a "lead" capable of acting on the target to cure the disease.[26] A target is often a single molecule, such as a gene or a protein, responsible in large part for triggering the disease. Once identified, it has to be tested and its role in the disease confirmed and

[25] *See* DiMasi et al., *supra* note 6, at 151-155; *see also* CYNTHIA HO, *From Conception to Commercial Success, in* ACCESS TO MEDICINE IN THE GLOBAL ECONOMY: INTERNATIONAL AGREEMENTS ON PATENTS AND RELATED RIGHTS 3, 6 (2011).

[26] *See* Teresa Brodniewicz & Grzegorz Grynkiewicz, *Preclinical Drug Development*, 67(6) ACTA POLONIEA PHARMACEUTICA 579 (2010), http://www.mtz-clinical.com/files/preclinical_drug_development.pdf.

validated.[27]

After the target has been validated, the drug originator has to find a promising molecule (a "lead compound") to act on the target in such a way as to inhibit the diseased condition. This is typically done by screening hundreds of thousands of chemical and biochemical substances that are likely to impact the target.[28] New leads have arisen either as a result of serendipity**,** or from analogy to the structures of known compounds. These may be natural ligands - enzyme substrates or receptor agonists, or they may be extant pharmacological agents - inhibitors or antagonists. In the context of ethno-biology, leads may also be found by isolating active compounds from traditional herbal remedies.[29] The lead compound, once identified is optimized for effectively reaching the target and staying in the body for a time long enough (pharmacokinetics)[30] to interact with the target and inhibit the disease (pharmacodynamics).[31]

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[27] *See* Jurgen Drews, *Drug Discovery: A Historical Perspective*, 287 SCIENCE 1960, 1962-1963 (2000). (explaining that validation is a step-wise process in which the role of a hypothetical target in relation to a disease phenotype is understood).

[28] *See* US FOOD AND DRUG ADMINISTRATION, *The Beginnings: Laboratory and Animal Studies, Information for Consumers (Drugs)*, http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143475.htm. (last visited Sept. 24, 2011).

[29] *See* DARREN R. FLOWER, MOLECULAR INFORMATICS: SHARPENING DRUG DESIGN'S CUTTING EDGE 16 (2002) (suggesting that many successful drugs such as Aspirin (originally derived from willow bark) were derived in this way).

[30] *See* Robert S. Porter et al., *The Merck Manuals Online Medical Library*, http://www.merckmanuals.com/professional/index/ind_ph.html, (last visited Sept. 24, 2011) (stating that pharmacokinetics, often described as what the body does to a drug, refers to the movement of drug into, through, and out of the body—and includes the course of its absorption, bioavailability, distribution, metabolism, and excretion.).

[31] *See id.* (stating that pharmacodynamics, often described as what a drug does to the body, involves receptor binding (including receptor sensitivity), post receptor effects, and chemical interactions.)

**2. Pre-clinical Phase**

The pre-clinical phase involves testing an optimized lead in the laboratory (in vitro)[32] as well as on animals to determine its preliminary safety and efficacy. The data generated through the above experiments is then used to file an Investigational New Drug Application (hereinafter "INDA"), an application requesting the US Food and Drug Administration's (hereinafter "FDA") permission to test the drug on human beings.[33] The EU follows a similar procedure, where prior to conducting human trials, the sponsor must request a Clinical Trial Authorisation (hereinafter "CTA").[34] After the relevant permission is granted, an IND/CTA applicant is entitled to initiate human trials, the most expensive stage in the drug development framework.

**3. Clinical Trial Phase**

The clinical trial phase entails three stages, each conducted on a progressively larger number of volunteers. Stage I of the clinical trials is carried out on a small

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[32] *See In vitro Definition,* MACMILLANDICTIONARY.COM, http://www.macmillandictionary.com/thesaurus/british/in-vitro#in-vitro_3 (last visited Sept. 24, 2011) (defining "in vitro" to mean something done or produced in a laboratory using a glass plate or test tube).

[33] *See* US FOOD AND DRUG ADMINISTRATION, *Investigational New Drug (IND) Application*, http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm (last visited Sept. 24, 2011).

[34] *See* LINDA FOSSATI WOOD, TARGETED REGULATORY WRITING TECHNIQUES: CLINICAL DOCUMENTS FOR DRUGS AND BIOLOGICS (2009) (stating that the CTA application includes a group of scientific documents called an Investigational Medicinal Products Dossier (hereinafter "IMPD")).

number (between 20 and 80) of healthy human volunteers, primarily to determine toxicity and appropriate dosage.[35] Stage II of the clinical trials is carried out on a larger number (between 100 and 300) of "diseased" participants in order to gather data on the drug's efficacy, along with further indications of side effects.[36] Finally, in Stage III, the drug is administered to a large number of volunteers (between 1,000 and 3,000), to firmly establish its efficacy, acquire more statistically significant results and determine the less common side effects.[37]

These steps are broadly similar to the EU regulatory process as well.[38] The trials culminate in the filing of a New Drug Application (hereinafter "NDA") before the drug regulator, which is then evaluated on several criteria, including the efficacy and safety of the drug in question, as also the severity of the disease in question.[39] Essentially, the FDA follows a risk-benefit analysis, wherein a drug is considered fit for approval, if its benefits outweigh the risks.[40] Often, drug applicants are subjected to a fourth phase as well, where they have to monitor the long-term use of the drug in specific patients, as well as the occurrence of rare side

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[35] *See* US FOOD AND DRUG ADMINISTRATION, *Inside Clinical Trials: Testing Medical Products in People*, http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143531.htm (last visited Sep. 24, 2011).

[36] *See id.*

[37] *See id.*

[38] *See* Valerie Junod, *Drug Marketing Exclusivity under United States and European Union Law*, 59 FOOD & DRUG L. J. 479 (2004).

[39] *See* Louis P. Garrison et al., *Assessing a Structured, Quantitative Health Outcomes Approach to Drug Risk-Benefit Analysis*, 26(3) HEALTH AFF. 684 (2007).

[40] *See id.*

effects.[41]

In short, the term "drug discovery" is used to refer to all stages involving the search for and identification of a disease target and the discovery of a lead to inhibit that target. "Drug development," on the other hand, effectively begins with the pre-clinical phase (when the lead is subjected to laboratory and animal testing) and includes, as its major component, the clinical trial phase (phases 1 to 3).

### B. Costs and Risks of Pharmaceutical Innovation

As can be inferred from the phases described above, the process of pharmaceutical innovation entails significant costs and a high risk of failure. It is estimated that less than 1% of the compounds examined in the pre-clinical phase make it to clinical trials.[42] Of the compounds that make it to clinical trials, only 19% procure FDA approval.[43]

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[41] *See* Alzhiemer Europe, *Phases of Clinical Trials*, *available at* http://www.alzheimer-europe.org/DE/Research/Understanding-dementia-research/Clinical-trials/Phases-of-clinical-trials (last visited Sept. 24, 2011).

[42] *See* Henry Grabowski, *Patents and New Product Development in the Pharmaceutical and Biotechnology Industries* 4 (July, 2002), http://www.dklevine.com/archive/grabow-patents.pdf; *see also* Aaron Xavier Fellmeth, *Secrecy, Monopoly and Access to Pharmaceuticals in International Trade Law: Protection of Marketing Approval Data under the TRIPS Agreement*, 45 HARV. INT'L. L. J. 443, 443-95 (2004).

[43] *See* Joseph A. DiMasi et al., *Trends in Risks Associated with New Drug Development: Success Rates for Investigational Drugs*, 87(3) CLIN. PHARMACOL. THER. 272 (2010); *see also* Pedro Cuatrecasas, *Drug Discovery in Jeopardy*, 116 J. CLINICAL INVESTIGATIONS 2837 (2006) (stating that, "Scientists and other professionals in the industry are poor in predicting complex responses to drugs . . . As a direct result, drug development remains part science and part art."); *see also* TAMAS BARTFAI & GRAHAM V. LEES, DRUG DISCOVERY FROM BEDSIDE TO WALL STREET 258 (2006).

The number of failures during drug development has been constantly on the rise in the recent past. During the period 2001-2006, the percentage of new products that were dropped after Stage II clinical trials (when drugs are first tested against a placebo) rose by 20%. During Stage III trials i.e. large-scale trials to test both safety and efficacy, the failure rate increased by 11%.[44] It is also pertinent to note that despite significant investments in R&D, the FDA approved only 19 first-of-their-kind remedies in 2007—the fewest since 1983—and only 24 in 2008.[45] It is estimated that half of all drugs that fail in late-stage trials drop out of the pipeline due to their inability to beat placebos.[46]

Apart from the high risks, the drug innovation process entails significant costs as well. The most cited study in this regard (hereinafter "DiMasi study") estimated that it would take approximately U.S. $802 million to produce a marketable drug.[47] These estimates have increased, with the most recent figure amounting to approximately U.S. $1.3 billion.[48] However, given that drug companies have been

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[44] *See* Steve Silberman, *Placebos Are Getting More Effective. Drugmakers Are Desperate to Know Why* (Aug. 24, 2009), http://www.wired.com/medtech/drugs/magazine/17-09/ff_placebo_effect?currentPage=all (last visited Sept. 30, 2011).

[45] *See id*

[46] *See id.*

[47] *See id*.

[48] *See* Pharmaceutical Research and Manufacturers of America, *Pharmaceutical Industry Profile 2010*, (Mar. 2010), http://www.phrma.org/sites/default/files/159/profile_2010_final.pdf (stating that the figure reported for the year 2006 was US $1.3 billion); *see also* Joseph A. DiMasi & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 MANAGE. DECIS. ECON. 469 (2007); *see also* Tufts Centre for Study of Drug Development, Backgrounder: A Methodology for Counting Costs for Pharmaceutical R&D (2001), http://csdd.tufts.edu./NewsEvents/RecentNews.asp?newsid=5 (last visited Sep. 24, 2011) (the first such study by the Tufts Center, in 1979 proclaimed that the true cost to develop a new drug was U.S.

reluctant to disclose their costs of drug discovery and development to the public, these costs remain a highly contested issue.

In 2001, Public Citizen, a civil society group in the U.S., contested the above figures on several grounds, the most pertinent of which are highlighted below:

i) R&D costs should be regarded as an expense and not an investment. Therefore, the costs of capital are irrelevant.[49]

ii) The estimated cost did not take into account the decrease in FDA review time, shorter clinical trial periods, and the contribution of new technologies such as genomics and combinatorial chemistry, which are believed to have assisted in the lowering of costs involved in creating drug leads.[50]

iii) If one were to assume the veracity of the pharmaceutical industry's self-reported total R&D figures between 1994 and 2000 and divide this amount by the

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$54 million, in 1976 dollars, in 1991, the Tufts Center updated the study and pegged the cost at U.S. $231 million, in 1987 dollars and finally, the figure for the year 2000 was U.S. $802 million).

[49] Some critics have asserted that there are no opportunity costs to pharmaceutical R&D because pharmaceutical firms "have no choice but to spend money on R&D if they wish to be in the pharmaceutical business." PUBLIC CITIZEN, *Rx R&D Myths: The Case against the Drug Industry's R&D "Scare Card"* 3, *available at* http://www.citizen.org/documents/rdmyths.pdf; *see also* MARCIA ANGELL, THE TRUTH ABOUT DRUG COMPANIES AND HOW THEY DECEIVE US (2005). *But see* Joseph A. DiMasi et al., *Assessing Claims about the Cost of New Drug Development: A Critique of the Public Citizen and TB Alliance Reports*, (2004), http://csdd.tufts.edu/files/uploads/assessing_claims.pdf (arguing that in view of the long development cycles inherent in pharmaceutical R&D, one cannot ignore the associated opportunity costs (including both out-of-pocket costs and capitalised costs) of the capital invested).

[50] *See* PUBLIC CITIZEN, *supra* note 49, at 4.

total number of approved drugs (after controlling for time lag), one would arrive at a figure of U.S. $108 million per new drug before tax benefits and U.S. $71 million after, which is significantly lower than what the DiMasi study cites.[51]

Donald Light additionally critiques the study on the ground that the numbers are based on a small sample of large pharmaceutical firms[52] which were non-randomly selected, and include only new molecular entities (hereinafter "NME"), the most costly sub-group of pharmaceuticals which constitute only one-third of new drug approvals.[53] He argues that if the costs of other "incremental" drugs (constituting three-fourth of all drugs) were taken into account, the average cost of a drug would fall to USD 400 million.[54] Light also offers several other correctives to argue in favour of a far lower cost estimate for clinical trials.[55] First, the number of subjects involved in clinical trials as per FDA data were about one-

[51] *See* Donald W. Light, *Misleading Congress About Drug Development,* 32 J. HEALTH POL., POL'Y & L. 895, 897 (2007) (stating that, "The Public Citizen team used a simple, back-of-the-envelope method for calculating R&D expenses, but this method is intuitively appealing.").

[52] *See id*. at 897-900 (noting that, "[T]he sample was non-random and small, using only ten firms. Originally, the researchers invited twenty-four firms, using unstated criteria, and twelve of them declined for unstated reasons. The other twelve corporations chose to participate, but two provided inadequate data.").

[53] *See* Light, *supra* note 51. *But see* Joseph A. DiMasi et al., *Misleading Congress about Drug Development – Reply*, 33 J. HEALTH POL., POL'Y & L. 319 (2008).

[54] *See* Light, *supra* note 51, at 896 (noting that, "If one-third of new drugs average U.S. $800 million in R&D costs and two-thirds average one-quarter of that cost, or U.S. $200 million, then should not the CBO point out that the overall average is only U.S. $400 million?"); *see also* U.S. CBO, *Research and Development in the Pharmaceutical Industry* 2 (Pub. No. 2589, 2006), www.cbo.gov/showdoc.cfm?index=7615&sequence=0 (last visited Sept. 24, 2011) ("Most new drug products have much lower R&D costs than NMEs because they are incremental improvements on existing drugs....Their average direct cost may be only about one-fourth that of an NME. Their opportunity costs are also lower due to the extent that they take less time to develop.").

[55] *See* Donald W. Light, *Reply to DiMasi, Hansen and Grabowsky*, 33 J. HEALTH POL., POL'Y & L. 325 (2008).

third or less than those used by DiMasi, suggesting that the rest of the trials were done by firms to primarily bolster their marketing materials.[56] Second, he cites data from the National Institutes of Health (NIH) indicating the costs per trial to be only a quarter of the figures used by DiMasi.[57]

Notwithstanding the veracity of DiMasi's figures, there is no gainsaying the fact that the conduct of clinical trials and the generation of data relating to safety and efficacy is an expensive process, when compared with the costs of market entry for other technology products such as electronics and software. The question of appropriately protecting these investments from free-riders is, therefore an urgent one that deserves serious consideration.[58]

### C. Declining Rates of Pharmaceutical Innovation

Pharmaceutical innovative output has been declining in the recent past.[59] While

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[56] *See id*. (noting the fact that private drug companies include legal and advertising costs in their R&D expenditure has also been critiqued); *see also* MICHELE BOLDRIN & DAVID K. LEVINE, AGAINST INTELLECTUAL MONOPOLY 237 (2005).

[57] *See* Light, *supra* note 55, at 326.

[58] The problem of free riding and the issue around appropriability that it generates is a recurring theme in the literature around patents and innovation. Illustratively, see Mark A. Lemley, *Property, Intellectual Property, and Free Riding*, 83 TEX. L. REV. 1031, 1035 (2005).

[59] *See* Matt Ridley, *Drugs That Are as Smart as Our Diseases*, (Sept. 17, 2011) http://online.wsj.com/article/SB10001424053111904265504576567070931547618.html (last visited Sept. 21, 2011) (stating that, "[T]he productivity of drugs coming out of clinical trials has been plummeting, and the cost per drug has been rocketing skyward. The more knowledge swells, the more pharmaceutical innovation fails.")

investments in pharmaceutical R&D have nearly tripled since 1995,[60] the number of truly new drugs, as measured by NMEs approved by the FDA and other regulatory agencies have fallen by close to 50% — from an average of 37 per year between 1995 and 1999 to an average of 21 per year between 2000 and 2010.[61] The U.S. Congressional Budget Office report notes that:

> Annual approvals of innovative new drugs— so-called new molecular entities—by the Food and Drug Administration (FDA) increased over the 1980s and peaked sharply in the mid-1990s but then experienced a pronounced six-year decline. In that decline, the total number of NMEs approved each year fell from a high of 53 in 1996 to 17 in 2002. The approvals rebounded to 36 by 2004 but fell again in 2005, to 20.[62]

Since then, the figure has hovered around this mark, the most recent being 25 approvals in 2009.[63] A recent report states that of the 97 new drugs approved in 2010, 74 provide little or no advantage. More problematically, 19 appear to possess greater risks than benefits. Of the remaining, 3 offer some clinical advantages, and only 1 counts as an important advance. Most tellingly, not a single one of the total

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[60] *See* National Science Foundation, Science and Engineering Indicators, 4-20 (2010), http://democrats.science.house.gov/Media/file/Reports/NSF_Science_and_Engineering_Indicators_2010_report.pdf (stating that pharmaceutical R&D (private sector) totalled U.S. $47.6 billion in 2007); *see also* National Science Foundation, Science and Engineering Indicators, App'x Tbl. 4-12 (2010), http://www.nsf.gov/statistics/seind10/append/c4/at04-12.pdf.

[61] *See* U.S. CBO, *supra* note 22 (noting that even with the drug industry's R&D spending rapidly increasing, the number of new drugs approved each year show little change and the average R&D cost per new drug has grown significantly).

[62] *See id. supra* note 22 (noting that on average, only about one-third of new drug applications submitted to the FDA are for NMEs and that most of the rest are either for reformulations or incremental modifications of existing drugs or for new "on-label" uses (additional health conditions for which an existing drug can be prescribed)).

[63] *See* Molly Redfield Ward, *Notes on the 2004 to 2009 United States Food and Drug Administration Approval of New Molecular Entities (NMEs)*, 4 (Knowledge Ecology International Research Note, 2010)*available at*, http://keionline.org/misc-docs/research_notes/kei_rn_2010_3.pdf.

97 could be said to represent a scientific breakthrough.[64] It is difficult to pinpoint the exact reason for this decline in innovative output. Some argue that this stems from the increasing complexity of modern day ailments, necessitating more resources, expertise and time in discovering new cures.[65] They point to escalating regulatory pressures[66] and the advent of generic competition as other factors adding to the costs and risks of drug discovery and development.[67]

Others are less forgiving, arguing that the pharmaceutical industry spends more money on marketing and less on real R&D.[68] Many also castigate the pharmaceutical industry for raising prices to unaffordable levels[69] and spending

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[64] *See 'New drugs and indications in 2010: inadequate assessment; patients at risk'* 31(328) REV PRESCRIRE 134-141 (2011), *available at* http://english.prescrire.org/en/960F30BC098B29D02641D9892EB36716/Download.aspx (last visited Sept. 21, 2011).

[65] *See* Fabio Pammolli et al., *The Productivity Crisis in Pharmaceutical R&D*, 10 NAT. REV. DRUG DISCOVERY, 428-438 (2011) (noting that apparently, the simplest problems have already been solved, and researchers are left with more difficult challenges, while the number of options that can yield viable therapies grow, raising the cost of exploring and developing new treatments).

[66] *See* Silberman, *supra* note 44; *see also* Bernard Munos, *Lessons from 60 years of Pharmaceutical Innovation*, 8 NAT. REV. DRUG DISCOVERY 959, 964 (2009).

[67] *See* Grabowski, *supra* note 42, at 91-92 ("Recently Prozac was subject to its first generic competition in September 2001. Prozac lost over 80 percent of its U.S. sales to generics within the first month after their entry."); *see also* Benjamin G. Druss et al., *Listening to Generic Prozac: Winners, Losers, and Sideliners*, 23(5) HEALTH AFFAIRS 210, 214 (2004) ("Purchasers saved 87 percent per tablet once Barr Laboratories' 180 day period of generic exclusivity on the drug expired.").

[68] *See* Dan Stober, *Researcher: Europe Surpasses United States in New Drug Discoveries,* http://news.stanford.edu/pr/2009/pr-light-pharma-study-082109.html (last visited Sept. 24 2011) (quoting Donald W. Light who said that, "High prices for these new drugs enable companies to spend 2.5 times more on marketing than on R&D to persuade physicians to prescribe them and patients to want them. Thus, current incentives reward better marketing over better value.").

[69] *See* Marcia Angell, *Excess in the Pharmaceutical Industry*, 171(12) CAN. MED. ASSOC. J. 1451 (2004); *see also* UNITED STATES GOVERNMENT ACCOUNTABILITY OFFICE, PRESCRIPTION DRUGS: TRENDS IN USUAL AND CUSTOMARY PRICES FOR COMMONLY USED DRUGS (Feb. 10 2011), http://www.gao.gov/new.items/d11306r.pdf; *see also After Makena: Could a Risk Corridors Approach Balance Incentives and Access?,* HEALTH LAW PROF BLOG, (Mar. 31, 2011),

more resources on the creation of "me-too" drugs[70] by a process referred to as "ever-greening".[71] Essentially, this involves tinkering with existing drug molecules and extending market monopolies by gaming the patent and regulatory regimes. And last, but not the least, critics point to the fact that despite its falling rate of innovative output, the pharmaceutical industry continues to remain one of the most profitable industries.[72]

All of this causes the public to perceive the industry as one that simply exploits the market, without spending adequate resources on finding new cures.[73] Given this sub-optimal rate and range of pharmaceutical innovation in the midst of rapidly escalating costs of new drugs, the question of incentives often takes centre stage. While the industry claims that the current patent regime offers insufficient protection,[74] public health advocates and scholars claim that the present patent

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http://lawprofessors.typepad.com/healthlawprof_blog/2011/03/after-makena-could-a-risk-corridors-approach-balance-incentives-and-access.html; *see also infra* text accompanying notes 387-396.

[70] *See* Huskamp, *supra* note 9.

[71] *See* Faunce & J. Lexchin *supra* note 10 and *infra* notes 452-455-441 and accompanying text.

[72] *See* David Henry & Joel Lexchin, *The Pharmaceutical Industry as a Medicines Provider,* 360 LANCET 1590 (2002) (noting that the pharmaceutical industry enjoys an average 16.2% profit, ahead of financial companies (11.6%) and beverages (10%)); *see also* Alberto Heimler, *The Pharmaceutical Industry and Parallel Trade*, *available at* www.wto.org/english/tratop_e/trips_e/hosbjor_presentations_e/31heimler_e.doc (last visited Sept. 24, 2011); *see also* Iain M. Cockburn, *The Changing Structure of Pharmaceutical Industry*, 23(1) HEALTH AFFAIRS 10, 14 (2004).

[73] *See* Angell, *supra* note 69.

[74] *See* International Federation of Pharmaceutical Manufacturers & Associations, *The Pharmaceutical Innovation Platform: Meeting Essential Global Health Needs*, 30 (2007), http://www.ifpma.org/fileadmin/templates/ifpmaissues/pdfs/IFPMA-PIP-Nov2007-Final-EN.pdf.

system over-rewards inventions and permits them to charge excessively high prices.[75] They cite the profitability of the pharmaceutical industry as living proof of this sentiment.[76] I intend to make a modest contribution to this debate by proposing an incentive regime that is more optimally suited towards fostering higher levels of pharmaceutical innovation. The next two Chapters explore the current incentive regimes, namely patents and data exclusivity, to demonstrate their shortcomings and to set the tone for the investment protection regime proposed in this thesis.

[75] *See* Aidan Hollis, *An Efficient Reward System for Pharmaceutical Innovation*, (2004), http://www.who.int/intellectualproperty/news/en/Submission-Hollis.pdf; *see also* Steven E. Landsburg, *The Mother-in-Law of Invention* (2000), http://www.slate.com/id/68674/ (last visited Sept. 24, 2011).

[76] *See* Angell, *supra* note 69.

## CH. II: PATENTS, INNOVATION AND INVESTMENT PROTECTION

### A. Patent Theories

The debates on innovation policy are inextricably woven with references to the patent regime, often seen as the primary legal incentive for technological innovation.[77] At its very core, the patent system seeks to foster new and non-obvious inventions by granting a limited legal monopoly.[78] The theories underlying the patent system are many, and I discuss the most important ones below.[79]

#### 1. Incentive Theory

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[77] *See* Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law,* 89 VA. L. REV. 1575, 1575 (2003) ("Patent law is our primary policy tool to promote innovation, encourage the development of new technologies, and increase the fund of human knowledge. To accomplish this end, the patent statute creates a general set of legal rules that govern a wide variety of technologies."); *see generally* WILLIAM D. NORDHAUS, INVENTION, GROWTH AND WELFARE: A THEORETICAL TREATMENT OF TECHNOLOGICAL CHANGE (1969) (discussing the standard economic theory of IP); *see also* Kenneth J. Arrow, *Economic Welfare and the Allocation of Resources for Innovation*, *in* THE RATE AND DIRECTION OF INVENTIVE ACTIVITY: ECONOMIC AND SOCIAL FACTORS 609 (William D. Nordhaus ed., 1962).

[78] *See* Hall, *supra* note 3, at 568 (defining patents as the legal right designed to protect property rights of an inventor in intangibles to exclude others from making or using a particular invention and stating that this right is customarily limited in time, to twenty years from the date of application submission in most countries). Hall states: "The principle behind the modern patent is that an inventor is allowed a limited amount of time to exclude others from supplying or using an invention in order to encourage inventive activity by preventing immediate imitation."; *see also* Gideon Parchomovsky & R. Polk Wagner, *Patent Portfolios,* 154 U. PA. L. REV. 1, 13-14 (2005) (discussing the standard justification for granting a limited legal monopoly to inventors by virtue of patents). They note:

> Absent patent protection, copiers would be able to appropriate much of the value embodied in inventions without incurring the considerable costs of research and development. In such a world, however, inventors would likely put their creative skills to rest and too few inventions would be produced. Patents remedy the appropriability problem that attends the production of information goods by bestowing upon inventors exclusive rights in the inventions they divined.

[79] *See* W. Fisher, *Theories of Intellectual Property*, *in* NEW ESSAYS IN THE LEGAL AND POLITICAL THEORY OF PROPERTY, 168–200 (S. R. Munzer ed., 2001).

The most prevalent justification for the patent system is offered by the "incentive" theory which stipulates that patent rewards (in the form of 20 year monopolies) incentivise prospective inventors to accelerate their inventive efforts, more than would be the case without patents.[80] In other words, patents are likely to increase the rate of generation of new and useful ideas for society. Although some may argue that new ideas and inventions are likely to be generated even without patents,[81] the key question to be answered is: would a patent regime accelerate the rate of emergence of new ideas and products based on them?

The prevalence of the incentive theory notwithstanding, it is yet to find strong empirical support.[82] Bronwyn H. Hall concludes that although a stronger

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[80] *See id*.; *see also, for e.g.,* U.S. CONST. art. 1, § 8, cl. 2 (acknowledging explicitly the incentive theory by providing that Congress has the power "to promote the progress of science and useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries."); *see also* Mazer v. Stein, 347 US 201, 219 (1954) ("The economic philosophy behind the clause empowering Congress to grant patents and copyrights is the conviction that encouragement of individual effort by personal gain is the best way to advance public welfare.")

[81] Notable examples of inventions that came about without the incentive of a patent include Zacharias Janssen, who invented the first compound microscope in 1595 and Johannes Gutenberg who is credited with inventing the first printing press. Michele Boldrin & David K. Levine, *Innovation without Patents*, *available at* http://www.dklevine.com/papers/ip.ch.4.m1004.pdf (stating that a number of historically important developments in the field of agriculture, electronics and cryptography took place even without patents).

[82] *See* E. Mansfield, *Patents and Innovation: An Empirical Study*, *in* MANAGEMENT SCIENCE 32, 2, 173-181 (1986); *see also* Andrew W. Torrance, & Bill Tomlinson, *Patents and the Regress of Useful Arts* (May, 28 2009); Columbia Science and Technology Law Review, Vol. 10, 2009.("despite the economic logic of the conventional view, there exists surprisingly little empirical evidence to support the key assumption that patents do actually spur technological innovation."); *see also* George Priest, *What Economists Can Tell Lawyers About Intellectual Property*, 8 RES. L. & ECON. 19 (1986)

patent system is likely to result in an increase in patenting, it is not clear if these changes will also simultaneously result in an increase in innovative activity.[83]

Apart from Hall's analysis, other studies have also pointed to the lack of strong empirical support for the innovation inducing rationale underling the patent regime. Illustratively, based on surveys of inventors in Britain and America in the nineteenth and twentieth centuries, Petra Moser suggests that most inventors preferred trade secrecy to patenting.[84] She cites a 1994 survey of 1,478 American manufacturing firms, where it was found that firms typically rely on a range of mechanisms, including patents, secrecy, lead-time, and the use of complementary assets to capture profits from their innovations. Of these mechanisms, patents were found to be the least important.[85] These findings resonate with the conclusions of the National Academies, which in its report titled "Patents in the Knowledge-Based Economy" noted that: "[t]here are theoretical as well as empirical reasons to question whether patent rights advance innovation in a substantial way in most industries."[86]

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[83] *See* Hall, *supra* note 3, at 574,

[84] *See* Petra Moser, *Why don't Inventors Patent?* 1 (NBER Working Paper, 2007), *available at* http://www.nber.org/papers/w13294 (arguing that the inventors' choice between patenting and secrecy represented a trade-off between a more "certain" protection for a finite period of time (through patent) and uncertain protection for a period which could last up to infinity (through secrecy)); *see also* Petra Moser, *What do Inventors Patent?* 8 (Working Paper, Aug. 1, 2004), *available at* http://www.utexas.edu/law/academics/centers/clbe/assets/Moser.pdf.

[85] *See* Petra Moser, *How do Patent Laws Influence Innovation: Evidence from Nineteenth Century World Fairs*, 12 (NBER Working Paper, 2003) *available at* http://www.nber.org/papers/w9909.pdf?new_window=1.

**[86]** See Committee on Intellectual Property Rights in the Knowledge Based Economy, NAT'L RESEARCH COUNCIL OF THE NAT'L ACADS., A PATENT SYSTEM FOR THE 21ST CENTURY 81–130

A later study under the aegis of the Berkeley Centre for Law and Technology (hereinafter "the Berkeley study"),[87] surveyed high-technology start-up firms in the U.S. and found that patents offer moderate to weak incentives to engage in core innovative activities.[88] The strength of the incentive depended in large part on the relevant technology sector in question; while patents helped start-ups in investment intensive sectors such as biotechnology become more competitive, they did not confer any significant advantage in sectors such as software.[89] The above studies appear to indicate that patents are relatively not that useful in securing competitive advantage and spurring accelerated innovation in most industries.

While assessing the role of patents, one must take note of the "social" costs of patents i.e. the fact that patents are capable of decelerating or slowing down innovative progress by "blocking" competition, particularly downstream research

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(Stephen A. Merrill et al. eds., 2004), *available at* http://www.nap.edu/catalog.php?record_id=10976.

[87] *See* Stuart J. H. Graham et al., *High Technology Entrepreneurs and the Patent System: Results of the 2008 Berkeley Patent Survey,* 24 BERK. TECH. L. J. 1255, 1287 (2010) (studying the impact of IP rights on entrepreneurship). They noted that, "because early-stage firms tend to lack the kinds of complementary assets (such as well-defined marketing channels, manufacturing capabilities, and access to cheap credit) that ease entry into the market, they are arguably even more sensitive to IP rights than their more mature counterparts."

[88] The survey questionnaire asked respondents to rate how strong or weak they found the patent incentive to be in respect of four innovation-related activities: "(a) inventing new products, processes, or services; (b) conducting initial research and development; (c) creating internal tools or processes to build or implement final products, processes, or services; and (d) undertaking the risks and costs of making, selling, and marketing a commercial product." *Id.* at 1283.

[89] It must be borne in mind that the Berkeley study was limited to assessing the competitive advantages of start-ups. *Id.* at 1280-1281.

and improvements.[90] This potential for blocking has been documented through specific historical examples in a seminal piece by Merges and Nelson[91] and in a later equally seminal piece by Heller and Eisenberg.[92] Merges and Nelson refer to broad patents covering technologies underlying Edison's light bulb, the Wright Brothers' airplane and Selden's automobile engine to buttress their claim that overbroad patents have retarded technological progress.[93]

It is pertinent to note that the term "blocking patents" is conventionally associated with dominant and subservient (dependent) patents, where the holder of the subservient patent requires a licence from the holder of the dominant patent and vice versa.[94] Such situations could be redressed by compulsory licensing

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[90] *See* Mark A. Lemley, *Rational Ignorance at the Patent Office,* 95 NORTHWESTERN U. L. REV. 1, 20 (2001) (discussing the rational ignorance at the patent office). He argues:

> The patent system intentionally restricts competition in certain technologies to encourage innovation. Doing so imposes a social cost, though the judgment of the patent system is that this cost is outweighed by the benefit to innovation…There is a great deal of literature attempting to assess whether that judgment is accurate or not, usually without success.

[91] *See* Robert P. Merges & Richard R. Nelson, *The Complex Economics of Patent Scope*, 90 COLUM. L. REV. 840, 885-887, 890-891 (1990).

[92] *See* Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anti-commons in Biomedical Research*, 280 SCIENCE698, 698–701 (1998).

[93] *But see* John Howells, *Patents and Downstream Innovation Suppression – Facts or Fiction? - A Critique of the Use of Historical Sources in Support of the Thesis that Broad Patent Scope Enables the Suppression or Hindrance of Downstream Useful-Technology Development* (2008), *available at* http://www.pucsp.br/icim/ingles/downloads/pdf_proceedings_2008/11.pdf (claiming that the treatment of these specific historical examples of blocking and the analysis by Merges & Nelson on this count is not sound); *see also* Walsh et al., *supra* note 3 (demonstrating that some of the fears around the potential for blocking in the biotechnology context, did not play out in actual practice); *see also* Heller & Eisenberg, *supra* note 92 (articulating some of the fears around the potential for blocking in the biotechnology context, which did not convert to reality).

[94] Blocking patents may arise when an improving innovation infringes a prior patent, while the innovator receives a separate patent on the improvements. Whether or

provisions, as is the case with some patent jurisdictions.[95] However, I use the term "blocking" in this thesis to refer more broadly to any situation where an upstream patent blocks or potentially blocks any downstream invention, whether or not the later invention is itself patented.[96]

Whilst assessing the role of the patent system in fostering innovation, scholars often point to the fact that significant investments and efforts may be required to translate inventive ideas into commercially useful products.[97] Indeed, an inventive idea has little use to the public, unless it has been developed into a marketable product.[98] While this developmental cost may be modest in some

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> not the improved product infringes the prior patent is determined by the breadth of its claims. Whether the improved product receives a patent is generally independent of this, and depends on whether the improvement is nonobvious or achieves the required inventive step.

Scotchmer, *infra* note 215, at 11; *see also* Robert Merges, *Intellectual Property Rights and Bargaining Breakdown: The Case of Blocking Patents*, 62 TENN. L. REV. 75, 81–82 (1994).

[95] Examples include the U.K. and India, as more fully discussed in a later Chapter. § 91 of the Indian Patents Act, 1970 provides for compulsory licensing in case of improvement patents. § 91 allows a person, who improves upon patented technology and registers such improvement as a patent to apply for a compulsory licence to work the said improvement, without infringing the original patent. *supra* text accompanying notes 588-598.

[96] Illustratively, consider the facts of Merck v. Integra*, infra* note 580, a case discussed in more detail in Chapter VI, pp. 169-170. The notion of blocking and hold up is particularly prevalent in the context of "trolls", now a term of art referring to an entity that owns and licenses patents, but does not work the patents itself; *see also* Troy L. Gwartney, *Harmonizing the Exclusionary Rights of Patents with Compulsory Licensing*, 50(4) WM. & MARY L. REV. 1395 (2008).

[97] *See* F.M. SCHERER, INDUSTRIAL MARKET STRUCTURE AND ECONOMIC PERFORMANCE, 440–41 (2d ed. 1980). (The traditional economic justification for patents has likely always encompassed the promotion of development and commercialization efforts in addition to inventive activity); *see also* Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J. L. & ECON. 265 (1977); *see also* John F. Duffy*, Rethinking the Prospect Theory of Patents*, 71 U. CHI. L. REV. 439, 440 (2004).

[98] *See* Ted Sichelman, *Commercializing Patents*, 62 STAN. L. REV. 341, 343 (2010) (citing examples of inventions that never translated to commercially viable productions such as the "anti-eating face mask" (disclosing a medieval-looking mask that prevents the wearer from eating), "beer bottle mini-

cases,[99] it is significant in others. But this by itself does not necessarily make out a case for patent protection. Firstly, it is possible that the technological product that is finally developed enjoys a significant lead-time over competitors and consequently a *de facto* market monopoly till such time as a rival enters the market.[100] Secondly, it might be the case that a competitor has to spend an amount equivalent to that of the original innovator in developing the product and is, therefore, dissuaded from entering the market.[101]

In other cases however, it is possible that the investments are significant, the lead-time advantages insufficient and the costs of making copies significantly lower than that of the originator product. Pharmaceutical drugs are an excellent example of this, where firms may be reluctant to invest in R&D, in the absence of some form of legally sanctioned market protection.[102]

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umbrella"(disclosing a "beerbrella," a small umbrella that attaches to a beer bottle to keep the bottle shaded) and "weed-cutting golf club" (disclosing a weed-whacker in the shape of a golf club)).

[99] *See* Jay Sorensens's coffee cup sleeve invention, *infra* note 159.

[100] *See* Robert Mazzoleni & Richard R. Nelson, *Economic Theories About the Benefits and Costs of Patents*, 32 J. ECON. ISSUES 1031, 1048 (1998) (asserting that patents are unnecessary they note that, "[I]n a wide range of circumstances….. [t]he advantages conferred by a head start . . . seem to provide ample incentive for the follow-on work."); *see also* Wesley M. Cohen et al., *Protecting Their Intellectual Assets: Appropriability Conditions and Why U.S. Manufacturing Firms Patent (Or Not)* 2-3 (NBER, Working Paper No. 7552, 2000), *available at* http://www.nber.org/papers/w7552.pdf. (noting that in many industries lead-time advantage is more effective than patents in recouping R&D investments).

[101] *See* F.M. Scherer, *Pharmaceutical Innovation* 27–28 (AEI–Brookings Joint Ctr., Working Paper No. 07-19, 2007), http://papers.ssrn.com/sol3/papers.cfm?abstract_id=902395 ("Even without patents, the firm that would seek to imitate the Boeing 787 would [end up] . . . spending very nearly as much as Boeing did to develop its 787.").

[102] Some scholars propose the institution of a separate commercialisation patent in order to incentivise the development of inventions. Sichelman, *supra* note 98.

For this reason, scholars such as Hall carve out an exception for the pharmaceutical industry, noting that that in such industries, patents are likely to increase investments and, thereby, the rate of innovative output as well.[103] I argue that if our expectation from the patent regime is that it fosters more investment and consequently increases the likelihood of more innovation being generated, then that function is more optimally achieved through a direct investment protection regime. In other words, rather than relying on a sub-optimal patent regime, I advocate the institution of a comprehensive investment protection regime.

**2. Prospect Theory**

In a seminal article, Edmund Kitch theorized that the patent system serves an important and previously unrecognized "prospect" function,[104] whereby it encourages investment in a technological prospect after the patent right has been granted.[105]

This theory is an offshoot of an early nineteenth century view that patents provide substantial *ex post* incentives to commercialize inventions, rather than

[103] *See* Hall, *supra* note 3, at 568.

[104] *See* Kitch, *supra* note 97.

[105] *See* Duffy, *supra* note 97.

merely *ex ante* incentives to invent.[106] The purported advantage of the prospect theory is that: (1) it allows "breathing room" for the inventor to invest in development of the prospect, without fear that another firm will pre-empt her in the market; and (2) it allows the inventor to co-ordinate the development of the technological prospect with interested third parties.[107]

To elaborate, Kitch believed that a patentee was best placed to scope out the relevant technological domain covered by the patent and develop it in an optimal manner, when compared with third party competitors. On this basis, he argued that patents help avoid the prospect of rivalrous waste engendered by a technological arena that was open to all. Kitch believed that a patentee with a broad patent was likely to either develop the technological prospect herself or to co-ordinate its development by licensing the invention to others.

Kitch's theory, therefore, supports the grant of a rather wide patent to the initial patentee or prospector.[108] However, Merges and Nelson question this "prospect" assumption[109] and demonstrate it to be empirically false through several notable historical examples, where patentees stifled the growth of the

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[106] *See* ARTHUR TWINNING HADLEY, ECONOMICS: AN ACCOUNT OF THE RELATIONS BETWEEN PRIVATE PROPERTY AND PUBLIC WELFARE 134 (1896) (arguing that the patent system "has established itself, not primarily as a stimulus for invention or disclosure," but as a driver of the investment of capital in the use and development of *pre-existing* inventions).

[107] *See* Merges & Nelson, *supra* note 91, at 871.

[108] *See* Duffy, *supra* note 97, at 440-441.

[109] *See* Merges & Nelson, *supra* note 91, at 872.

technological field by leveraging their broad patent monopolies, particularly in areas of technology characterised by cumulative innovation.[110]

Based on these examples, Merges and Nelson advocate that law should attempt to favour a competitive environment for improvements, whilst at the same time ensuring that the pioneer firm's incentives are not significantly reduced. In many industries, the efficiency gains from the pioneer's ability to coordinate through broad patents are likely to be outweighed by the loss of competition for improvements to the basic invention.[111] They argue that one potential way to achieve this fine balance is by tailoring patent scope appropriately and leaving sufficient room for improvements and for follow-on innovators. A recent piece of scholarship notes that another potential solution is to appropriately tailor patent remedies such as compulsory licensing.[112]

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[110] *See* Merges & Nelson, *supra* note 91, at 885-887, 890-891 (discussing the specific examples of the Edison light bulb patent, the Wright Brothers airplane patent and the Selden automobile patents to buttress their claim that overbroad patents in these contexts retarded technological progress); *but see* Howells, *supra* note 92, at 432 (questioning the analysis by Merges & Nelson that overbroad patents granted to the Wright brothers, Selden and Edison were responsible for the stunting of technological growth).

[111] *See id.* at 843 ("[T]he notion of a patent's social costs should include its potential to reduce competition in the market for improvements to the patented technology.").

[112] *See* John M. Golden, *Complex Economics and Patent Remedies,* 1(2) IP THEORY 50, 50 (suggesting that proper remedies for patent infringement are intrinsically related to the inefficiencies of patent rights as such). Golden argues:

> Current debates over the proper remedies for patent infringement have a strong relation to Merges and Nelson's concerns with potential dynamic inefficiencies of patent rights. One not-so-subtle insight underlying modern remedies debates is that, even if follow-on activity infringes a patent's scope, the patent might do little to limit that activity if remedies for patent infringement are sufficiently limited. If courts rarely issue injunctions to enforce patents and rarely issue damage awards that are more than a small fraction of an infringement profits, even broad patents on fundamental innovations might not significantly chill follow-on innovation.

Merges and Nelson argue that although such narrow patents may lead to rivalrous waste, as several competitors would enter the same technological arena and attempt to work on similar inventions, the same is likely to be outweighed by the creation of a competitive environment that would in turn engender higher levels of innovative output.[113] Their belief (as validated by historical examples) is that a single patentee was likely to be less committed to developing the prospect by herself. Further, they also argue that the prospect of effective co-ordination by the patentee to help develop the prospect by licensing the invention to third parties is not very high, owing to the high transaction costs involved.[114]

One must, however, note that Merges and Nelson do not question the wisdom of the patent system.[115] Rather, they merely question the validity of the

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[113] *See* Merges & Nelson, *supra* note 91, at 908.

[114] *See id*. at 877 (acknowledging that their proposition is open to criticism). They argue:

> Undoubtedly our position is open to criticism. Rivalry no doubt causes waste. Yet we have little faith in the imagination and willingness of a "prospect" holder to develop that prospect as energetically or creatively as she would when engaged in competition. We are also skeptical about her ability to orchestrate development. Given the way humans and organizations think and behave, we believe we are much better off with considerable rivalry in invention than with too little.
>
> Can we prove it? We can present empirical evidence that the granting of broad patents in many cases has stifled technical advance and that where technical advance has been rapid there almost always has been considerable rivalry.

[115] Some readers may interpret the position we have detailed above as a reflection of an antipatent bias on our part. Not so. While it may seem at first blush that any reduction in patent scope -- indeed, any lessening of the patentee's potential reward -- may severely undercut the incentive to invent, we do not believe this is the case…. Ultimately it is important to bear in mind that every potential inventor is also a potential infringer. Thus a "strengthening" of property rights will not always increase incentives to invent; it may do so for some pioneers, but it will also greatly

prospect theory and the assumption that broad patent rights would be optimally used by a patentee to either develop the technological field herself or to licence out her invention to those third parties who would develop the prospect in a coordinated fashion.[116]

### 3. Disclosure Theory

Some theorists advocate that the purpose of the patent system is best gleaned from the "bargain" or a "social contract" theory—i.e., an inventor who discloses details of her new invention is granted a state sanctioned monopoly of twenty years in return for such disclosure.[117] This theory rests on the assumption that were it not for patents, the putative patentee might have considered it more optimal to lock the invention away as a trade secret, thereby, depriving the society of important scientific knowledge.

In short, the promise of a patent incentivises the disclosure of important

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> increase an improver's chances of becoming enmeshed in litigation. Indeed this is the very heart of our case.

Merges & Nelson, *supra* note 91, at 916.

[116] *See* Arti Rai, *Fostering Cumulative Innovation in the Biopharmaceutical industry: The Role of Patents and Antitrust*, 16 BERK. TECH. L. J. 813 (2001) (arguing that, contrary to Kitch, a monopolist cannot be expected to co-ordinate further downstream product development through licensing; rather it would be more beneficial to have several competitors in this market); *see also* Sichelman *supra* note 98, at 345 (noting that such a "property-rights approach" as proposed to Kitch "can often retard commercialization").

[117] *See* Pfaff v. Wells Electronics Inc., 525 U.S. 55, 63 (1998) ("The patent system thus embodies a carefully crafted bargain for encouraging the creation and disclosure of new, useful, and non obvious advances in technology and design in return for the exclusive right to practice the invention for a period of years"); *see also* Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141, 150–51 (1989).

technological and scientific information that is of value to society.[118] Scholars skeptical of this theory argue that patent applications often hide more than what they reveal and that society does not really benefit from such disclosures to an extent sufficient enough to warrant the grant of a 20 year monopoly.[119] In a stinging criticism of the failure of the disclosure function of the patent system, a commentator opines that the dissemination of information is severely deterred either due to inadequate disclosure in the patent application or due to the threat of patent infringement suits which arise because of strict conditions on the "use" of the disclosed information.[120]

It is important to appreciate that the above criticism is not one that thwarts the core essence of the disclosure theory. If the concern is that patentees do not disclose their invention sufficiently for strategic reasons, one must insist on a more rigorous application of disclosure norms.[121] Secondly, the problem of strategic non-reliance on patent disclosures owing to future prospects of law suits claiming

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[118] *See* Kesan & Banik, *infra* note 235, at 23 ("Patents also encourage the dissemination of information about new inventions, thus permitting competitors to build upon or develop improved versions of patented inventions.").

[119] *See* Benjamin Roin, *The Disclosure Function of the Patent System (or Lack Thereof'),* 118 HARV. L. REV. 2007, 2008 (2005).

[120] *See id.* at 2007, 2008, 2019-2025.

[121] *See* Sean B. Seymore, *The Teaching Function of Patents*, 85 NOTRE DAME L. REV. 621, 627 (2010) (arguing in favour of strong disclosure and stating that the heightened standard of disclosure will bridge the gap between patent law and the norms of science which will likely induce innovators to turn to patents for substantive technical information). He further states: "[a]dopting the heightened disclosure framework will transform patents emerging from industrial research into readable teaching documents, which may become rich repositories of useful technical knowledge"); *see also* Lisa Larrimore Ouellette, *Do Patents Disclose Useful Information?*, 25(2) HARV. J. L. & TECH. 531 (2012), http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1762793 (explaining that there are substantial benefits for a strong patent disclosure).

willful infringement and damages is one that is largely specific to the US.[122]

In the pharmaceutical context, it is important to appreciate that even without disclosure through patent documents, the ultimate innovation that emerges from the patent would in many cases be self-disclosing i.e. amenable to reverse engineering.[123] The patent disclosure would, at best, permit society to have knowledge of an invention at an earlier point in time. However, it is not known whether such early disclosure could be equally incentivised through the promise of reputational gains through publications or other upstream incentives as discussed in Chapter VI.[124] Further, even assuming that there is some merit in an early disclosure, one has to ask if this advantage is sufficient to offset the disadvantages associated with the patent system, including its significant costs and the potential to block downstream research.

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[122] *See* Jeanne C. Fromer, *Patent Disclosure,* 94 IOWA L. REV. 539, 2009 (Patent infringement in the U.S. is akin to a strict-liability offense, but a court has the authority to award up to treble damages to a patentee when it finds an infringer to have acted "willfully". Therefore, firms, not willing to pay treble damages and being aware of the willful infringement rule routinely advise their employees not to read outside patents, thereby avoiding the risk of any knowledge of relevant patents and thus any willful infringement); *see also* Mark A. Lemley & Ragesh K. Tangri, *Ending Patent Law's Willfulness Game*, 18 BERK. TECH. L. J. 1085, 1100-02 (2003) (stating that the first significant cost relating to the willfulness game is its interference with the disclosure function of patent law.) They argue: "[t]he mere existence of the willfulness doctrine in its current form means that any time an individual or company learns of a patent that might be relevant to its products, the company is in trouble."; *see also* Ouellette, *supra* note 121.

[123] [T]he kind of innovation that lends itself to patent protection is typically vulnerable to reverse engineering. Once these inventions come into being and are brought to market, disclosure is inevitable. For this reason, disclosure is subsumed within patent law's larger purpose, which is to create a property regime that solves the public goods dilemma. Viewed in this light, one can appreciate why disclosure should be viewed as an ancillary benefit of the patent system, rather than a primary concern.

Alan J. Devlin, *The Misunderstood Function of Disclosure in Patent Law*, 23 HARV. J. L. & TECHN. 401 (2010).

[124] *See supra* text accompanying notes 568-569.

## 4. Labour Theory

The labour theory draws from John Locke's philosophy that a person who expends effort upon resources that are either un-owned or "held in common" has a natural property right to the fruits of her efforts – and that the state has a duty to respect and enforce this natural right.[125] In its application to intellectual property, one might argue that the pertinent raw materials (known ideas and concepts) are "held in common" and such raw materials when converted to useful technological innovations through the active deployment of labour ought to be protected as the property of the inventor.[126] Some scholars are, however, skeptical of this linkage and contend that Locke's theory relates only to real and physical property.[127] William Fisher states that since it is difficult to ascertain Locke's original intent, one cannot make out a determinative case for the protection of intellectual property from Locke's original theory.[128]

Locke laid down certain pre-conditions for the protection of property, widely known as the "Lockean provisos". The first proviso states that one is entitled

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[125] *See* JOHN LOCKE, SECOND TREATISE IN TWO TREATISES OF GOVERNMENT (Peter Laslett ed., 1988); *see also* Fisher, *supra* note 79, at 170.

[126] *See* Justin Hughes, *The Philosophy of Intellectual Property,* 77 GEO. L.J., 287, 299-330 (1988); *see also* Andrew R. Sommer, *Trouble on the Commons: A Lockean justification for Patent Law Harmonisation* 87 J. PAT. & TRADEMARK OFF. SOC'Y 141, 155 (2005); *see also* Benjamin G. Damstedt, *Limiting Locke, A Natural law Justification for the Fair Use Doctrine,* 112 YALE L. J. 1179 (2003).

[127] See John Meyer, *Nature, Property, and Democracy in the Debate over Genetically Modified Organisms* 8 (Paper No. 23, 2006), *available at* http://www.sss.ias.edu/files/papers/paper23.pdf.

[128] *See* Fisher, *supra* note 79.

to an exclusive right to a creation from the commons only when there is enough, and as good left in the commons for others.[129] The second proviso prohibits spoilage i.e. taking more from the commons than what one really needs, thereby, resulting in wastage.[130] In other words, one must not only leave enough apples in the orchard for others, but also refrain from taking home an excess quantity and letting them spoil.

Hettinger argues that intellectual property is incapable of meeting these two pre-requisites.[131] The first proviso relating to leaving enough and as good in the commons for others is not met, since patent grants vest the original inventor with an exclusive right to make, use and sell the invention. Subsequent inventors who independently come up with the same invention are prevented from using it or commercialising it. In this way, the first patent grant deprives the second independent inventor of a part of the commons.[132]

In so far as Locke's second proviso prohibiting wastage is concerned, Hettinger argues that the grant of intellectual property rights prevents certain beneficial third party use of products covered by such rights. In other words, but for such rights, others might have used and even improved upon the inventions or

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[129] *See* LOCKE, *supra* note 125, at 288.

[130] *See id.*

[131] *See* Edwin C. Hettinger, *Justifying Intellectual Property,* 18(1) PHILOSOPHY AND PUBLIC AFFAIRS 44-45 (1989).

[132] *See id.* at 44.

creations without the intellectual property owners' permission. The degree of such waste depends on how beneficial these products would have been to those who are excluded from their use as a result.[133]

From the Lockean theory, it is also not clear as to what counts as intellectual labour. Fisher finds at least four plausible candidates: (1) time and effort (for e.g., hours spent in front of the computer or in the laboratory); (2) activity in which one would rather not engage (for e.g., hours spent in the studio when one would rather be sailing); (3) activity that results in social benefits (for e.g., working on socially valuable inventions); (4) creative activity (i.e. the production of new ideas). Fisher opines that the first one may be closest to Locke's original intent.[134] However, if this were the case, most intellectual property regimes, which deny protection to mere labour, would be at odds with this theory.[135]

Fisher also argues that the act of mixing labour with the commons does not, under any of the various intellectual property regimes, work the way Locke envisaged real property to work. Firstly, under the Lockean theory, when one mixes one's physical labour with a plot of virgin land, one acquires a natural right to not only the crops produced, but the land itself. By contrast, when one mixes one's

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[133] *See id.* at 45.

[134] *See* Fisher, *supra* note 79. .

[135] *See* Wendy J. Gordon, *Intellectual Property*, *in* THE OXFORD HANDBOOK OF LEGAL STUDIES 625 (Peter Can & Mark Tushnet eds., 2003), http://ssrn.com/abstract_id=413001.

intellectual labour with an existing idea, one acquires an exclusive right only to the "original" or "novel" material generated, and not to the idea which was earlier part of the commons and which one had used to create the original or novel idea.[136]

Secondly, the set of entitlements that come with an intellectual property right are not the same as the ones envisaged by Locke for real property. Illustratively, the issuance of a patent on a mousetrap prevents others from making that mousetrap, but not from reading the patent and using the information contained therein to make an even better mousetrap. The issuance of a copyright on a novel prevents others from copying it, but not from reading it, discussing it or parodying it.

This issue is closely connected with the issue of "rivalry" and "exclusivity". While physical property is characterised by its rivalrous and excludable nature (wherein only one person can possess it and enjoy it to the fullest extent at any given point of time), intellectual property is non-rivalrous and non-excludable, and the same good can be enjoyed by several people at the same time, without in any way diminishing the others' possession or enjoyment of it.[137]

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[136] *See* Fisher, *supra* note 134, at 26.

[137] *See* Seana Shiffrin, *Intellectual Property, in* A COMPANION TO CONTEMPORARY POLITICAL PHILOSOPHY, 659 (Robert E. Goodin et al. eds., 2007), *available at* http://cdn.law.ucla.edu/SiteCollectionDocuments/faculty/shiffrin-intellectual%20property.pdf.

Yet another critical distinction between the two is one of temporality. While Locke suggests that real property rights would last forever, in that they are alienable, divisible, and inheritable indefinitely, most intellectual property rights are temporal and last only up to a certain number of years.[138]

Lastly, Fisher rightly points to the issue of proportionality. Even assuming that the Lockean theory would have supported the grant of patents, ought all inventions to be granted the same time period of protection or should it vary according to the importance of the invention? Illustratively, should Viagra, the brand name of a drug for treating male erectile dysfunction (hereinafter "MED") merit the same period of protection as a newly discovered drug to cure Tuberculosis (hereinafter "TB")?[139] Fisher suggests that Lockean theory provides no answer to such questions.[140]

**5. Personality Theory**

The personality or the personhood theory, derived, in large part, from the writings of Immanuel Kant and Georg Wilhelm Friedrich Hegel, postulates that private property rights are critical for the satisfaction of certain fundamental human needs.

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[138] *See* Fisher, *supra* note 134, at 26.

[139] *See* U.S. GLOBAL HEALTH POLICY PROGRAM, THE GLOBAL TUBERCULOSIS EPIDEMIC (Publication No. 7883-04, June 2010), http://www.kff.org/globalhealth/upload/7883-02.pdf.

[140] *See* Fisher, *supra* note 134, at 28.

In its application to intellectual property, one has to first identify the specific needs or interests that one wishes to promote through property rights.[141]

Jeremy Waldron suggests an illustrative list: property rights may be necessary to promote privacy; to enable persons to become self-reliant; to enable persons to help shape their social environments and establish their place in communities; to enable persons to assert their will and to be recognized as free agents by others; to promote security and leisure; to promote responsibility; to establish a sense of self-worth; to express ideas and to participate effectively in polity.[142]

Drawing on the above, Justin Hughes argues that legal protection ought to be accorded to the fruits of highly expressive intellectual activities, such as the writing of novels, rather than the fruits of less expressive activities, such as genetic research. This is because different categories of intellectual property seem to lend themselves to different amounts of "personality." For instance, poetry lends itself to personality better than trade secrets and symphonies better than microchip masks etc.[143] He also argues that because a person's "persona", his "public image, including his physical features, mannerisms, and history", is an important

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[141] *See id.*

[142] *See* Fisher, *supra* note 134, at 29-30.

[143] *See* Hughes, *supra* note 126, at 339.

"receptacle for personality," it deserves generous legal protection, despite the fact that ordinarily it does not result from labour.[144]

Lastly, he states that, "[a]uthors and inventors should be permitted to earn respect, honour, admiration, and money from the public by selling or giving away copies of their works, but should not be permitted to surrender their right to prevent others from mutilating or misattributing their works."[145]

Fisher, however, argues that the images of "personhood" that underlie most avatars of the personality theory are too abstract and thin to provide answers to many specific questions.[146] He suggests a more comprehensively articulated vision of human nature that would forthrightly address grand questions such as the importance of creativity to the soul.[147]

The theory has also been critiqued on the ground that it is yet to adequately address "fetishism" or "bad object relations," an aspect most persuasively argued by Margaret Radin.[148] The term "fetishism" was coined in the late 1800's and originates from the Portuguese word, *feitico,* meaning "obsessive fascination".

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[144] *See* Hughes, *supra* note 126, at 340.

[145] *See* Hughes, *supra* note 126, at 330-350.

[146] *See* Fisher, *supra* note 134, at 32.

[147] *See id.*

[148] *See* Margaret Jane Radin, *Property and Personhood,* 34 STAN. L. REV. 957 (1982).

Fetishistic arousal is generally considered problematic when it interferes with normal sexual or social functioning.[149]

In this context, Radin feels that we must construct sufficiently objective criteria to identify close object-relations (i.e. relations arising when the person is bound up with the object to a great extent) that should be excluded from recognition as personal property because the particular nature of the relationship works to hinder rather than to support "healthy" self-constitution. A key to distinguishing these cases is to examine the relationship between person and object through the lens of "health" i.e. one can tell the difference between personal property and fetishism in much the same way that one can distinguish between a healthy person and a sick person, or between a sane person and an insane person.

Fisher, however, critiques such attempts to distinguish between personal property and fetishism on the basis that it is very difficult to determine which of the many tastes exhibited are to be encouraged and which ones discouraged:[150] the quest for individuality?; or the hunger for fifteen minutes (or more) of fame? Yearnings or orientations of this nature are implicated by intellectual property

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[149] *See* *Fetishism*, PSYCHOLOGY TODAY (2005), http://www.psychologytoday.com/conditions/fetishism.

[150] *See* Fisher, *supra* note 134, at 32.

disputes. Determining which one of these aspects deserves protection is essential to assessing how those disputes might be resolved.[151]

Seana Shiffrin argues that a term of copyright that extends beyond the author's life does not comport well with the argument that one needs control over property in order to develop and assert one's personality publicly. She states that concerns for the reputation and the communicative intention of the dead does not, by itself, provide sufficient reason to impede the expressive, personality-building opportunities of the living. Personality rights theorists would need to explain why priority should be given to the expressive interests of original creators over others (and for how long), since others may wish to express themselves through the uninhibited use of intellectual works.[152]

### B. Pharmaceutical Patents and Innovation

The above discussion notes that the various justifications advocated for the patent system are far from persuasive. In particular, the "incentive" theory, often the most widely cited and relied upon, fails to drum up persuasive empirical evidence in its support. However, scepticism about the nexus between patents and innovation notwithstanding, most ardent critics readily admit that the pharmaceutical industry

[151] *See id* at 33.

[152] *See* Shiffrin, *supra* note 137, at 660.

is an exception.[153] Illustratively, Bessen and Meurer, two of the most vocal critics of the patent system note that, "In some industries, such as pharmaceuticals, patents provide strong positive incentives to invest in innovation. But in many other industries, perhaps most, patents fail to perform like property and they may actually discourage innovation."[154]

Courts have also endorsed similar sentiments while adjudicating upon the validity of pharmaceutical patents. "We have long acknowledged the importance of the patent system in encouraging innovation. . . . Importantly, the patent system provides incentive to the innovative drug companies to continue costly development efforts."[155] Implicit in the above statements are two assumptions:

1. That a greater amount of investment in R&D will yield higher levels of innovation;
2. That the patent system is optimally suited towards fostering higher levels of R&D investment.

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[153] *See* Federal Trade Commission [hereinafter FTC], *To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy,* 30, 34–41, 44, 50–55 (2003) *available at* http://www.ftc.gov/os/2003/10/innovationrpt.pdf (noting the prevalent perception of scholars that drug development is "the paradigm of patents spurring innovation."); *see also* William Kingston, *The Unexploited Potential of Patents, in* DIRECT PROTECTION OF INNOVATION 9, 30–32 (William Kingston ed., 1987) (concluding that patents fail to adequately promote innovation in most fields other than chemicals and pharmaceuticals, where the "invention-innovation link is . . . strong.").

[154] *See* Bessen & Meurer, *supra* note 3.

[155] *See* Sanofi-Synthelabo v. Apotex. Inc., 470 F.3d 1368, 1383 (Fed. Cir. 2006), *appeal docketed*, No. 2007-1438 (Fed. Cir. Sept. 4, 2007); *see also* Pfizer Canada Inc. v. Apotex Inc., 2009 FCA 8, [2009] 4 F.C.R. 223 (noting that "[t]he patent system is intended to provide an economic encouragement for research and development. It is well known that this is particularly important in the field of pharmaceuticals and biotechnology.").

It is difficult to quibble with the first sentiment, as it is logical to assume that, *ceteris paribus,* in an industry characterised by expensive R&D such as pharmaceuticals, a higher rate of investment is likely to accelerate innovative output.[156] However, the second assumption calls for a critical examination. For, if investment protection is the goal, it ought not to depend upon whether or not the underlying idea behind the drug is "new" and "inventive",[157] the two central tenets of patent law.[158] Rather, any drug that makes it past the regulatory filter ought to be entitled to such protection, since the discovery and development of all approved drugs entail significant investment.

### C. The Inadequacy of Patents

[156] *See* Merges & Nelson, *supra* note 91, at 871, 916 (noting rightly that, "increases in research and development expenditures yield more inventions.").

[157] Almost all patent regimes premise the grant of a patent on a demonstration that the claimed invention is new and non-obvious to a person skilled in the art. This requirement has been articulated in Article 27.1 of the TRIPS Agreement as well, which mandates that every invention which is new, inventive and useful shall be granted a patent. Agreement on Trade-Related Aspects of Intellectual Property Rights art. 27.1, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, Legal Instruments—Results of the Uruguay Round, 1869 U.N.T.S. 299, 33 I.L.M. 1195 (1994); *see also* CARLOS CORREA, TRADE RELATED ASPECTS OF INTELLECTUAL PROPERTY RIGHTS: A COMMENTARY ON THE TRIPS AGREEMENT 273 (1st ed. 2007).

[158] *See* Bonito Boats, Inc. v. Thunder Craft Boats, Inc. 489 U.S. 141 (1989) (underlining that the novelty and non-obviousness requirements "are grounded in the notion that concepts within the public grasp, or those so obvious that they readily could be, are the tools of creation available to all."); *see also* R. S. Eisenberg, *Analyze This: A Law and Economics Agenda for the Patent System,* 53 VAND. L. REV. 2081, 2088 (2000) ("Granting patents on technologies that are not new would impose the social costs of monopolies without the countervailing benefits of promoting development and introduction of welfare enhancing inventions.").

Patent regimes which aim to protect new and non-obvious inventions are not intrinsically suited towards the protection of investments underlying the creation of innovative products. The various deficiencies in this regard are outlined below:

**1. The Patentability Threshold**

That patents, in their current format, do not always translate into optimal investment protection instruments is evident when one considers the simple fact that several patented ideas and, products based on them may have emerged with meagre investment.[159] As a corollary, an idea, though widely known, may still require significant investment before being converted into a useful product. Illustratively, a molecule that is either known (through publication in scientific journals) or obvious in the light of prior art and therefore, not patentable may still entail extensive development costs (associated with clinical trials and the like) prior to being converted to a marketable drug.[160]

Consider the case of Pfizer's patent covering Sildenafil Citrate, a known PDE

[159] *See* U.S. Patent No. 5425497 (filed June 20, 1995) (relating to Jay Sorensens's coffee cup sleeve, a simple invention that would have incurred minimal costs of development); *see also* Barton, *supra* note 4, at 475-508 (describing a series of similar patents that have issued on insulating sleeves for paper -- he takes issue with such patents on grounds of economic theory, arguing that since such inventions were cheap to discover and develop, they would have emerged even without the prospect of patents).

[160] *See* Roin, *supra* note 2, at 553-4. ("Under the novelty requirement, negligible disclosures can prevent—and have prevented—socially valuable drugs from being patented.").

VA inhibitor[161] that turned out to be a path-breaking treatment for male erectile dysfunction (MED) and was voted as one of the brightest British innovations of the 1990's.[162] Viagra, Pfizer's brand name for the active ingredient, Sildenafil Citrate, was the first effective oral treatment for MED, now prescribed in more than 90 countries worldwide and is by far the most widely used treatment for the condition and highly effective, with up to 82% of patients experiencing benefits.[163]

At the time of this path-breaking discovery, Sildenafil Citrate was already a known substance and was being tested by Pfizer for its ability to cure angina (blood pressure) and a specific form of heart ailment. Upon discovering its potential new use as a cure for MED, Pfizer immediately filed a patent application.[164] The U.K. courts, however, invalidated the patent on the ground that the new use would have

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[161] The PDE VA inhibitor is a specific kind of phosphodiesterase inhibitor with a highly pronounced relaxant response. The use of Sildenafil Citrate as a PDE VA inhibitor was found to induce a pronounced and significant erectogenic effect in patients with an erectile dysfunction. C.G. Stief, *Phosphodiesterase Inhibitors in the Treatment of Erectile Dysfunction*, 36(2-3) DRUGS TODAY 93, (2000) *available at* http://journals.prous.com/journals/servlet/xmlxsl/pk_journals.xml_summary_pr?p_JournalId=4&p_RefId=568782&p_IsPs=N .

[162] *See* Lilly Icos Llc v. Pfizer Ltd (1) [2002] EWCA Civ. 1, *available at* http://www.bailii.org/ew/cases/EWCA/Civ/2002/1.html (last visited Jan. 18, 2011) (citing the article in the Times entitled, *Viagra earns Dome place as Best of British,* published on Apr. 20, 1999 which stated that "Viagra has won a place as one of the brightest British innovations of the 1990s.").

[163] *See* Darren R. Flower, *Molecular Informatics: Sharpening Drug Design's Cutting Edge*, 17 (2002) *available at* http://www.rsc.org/ebooks/archive/free/bk9780854048168/bk9780854048168-00001.pdf.

[164] Sildenafil Citrate essentially works by inhibiting an enzyme that retards the relaxation of the penile muscle. The relaxation of penile smooth muscle is traceable to chemicals called cyclic adenosine monophosphate or cAMP and cyclic guanosine monophosphate or cGMP. cGMP and cAMP are rendered ineffective by the action of a PDE enzyme. Viagra helps restore the potency of cGMP and cAMP by inhibiting the PDE enzyme with the help of certain other chemicals called PDE inhibitors.

been obvious to a person skilled in the art.[165] The court based its reasoning on the ground that the prior art included an article by Rajfer et al. and published patents,[166] that when combined would teach that Sildenafil Citrate, a known PDE VA inhibitors could be useful for the treatment of MED.[167]

Although the claimed invention was held obvious under English patent law, it is important to appreciate that the development of Sildenafil Citrate into a marketable drug would have required the infusion of significant investment in terms of time, effort and money. Unfortunately, current patent standards do not permit such investments to be protected.[168] As a commentator rightly notes:

> The novelty and non-obviousness requirements make no concession for the development costs of inventions and thus cause patents to be withheld from drugs that are unlikely to reach the public without that

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[165] *See* Lilly Icos Llc v. Pfizer Ltd [2002] EWCA Civ. 1 where the Court of Appeal in the U.K. upheld the High Court decision delivered by Laddie, J., in this regard (Pfizer Ltd v. Lilly Icos Llc [2000] EWHC Patents 49).

[166] Two earlier Pfizer patent applications, namely EP 0463 756 and EP 0526 004, referred to respectively as Bell I and Bell II, covered Sildenafil Citrate, along with a number of other chemicals, proposing their use for a number of medical applications, but not the treatment of MED specifically. However, these patents disclosed the use of Sildenafil Citrate as a PDE inhibitor for the treatment of such complaints as angina and hypertension.

[167] *See* Lilly Icos Llc v. Pfizer Ltd. [2002] EWCA Civ. 1, ¶ 54 *available at* http://www.bailii.org/ew/cases/EWCA/Civ/2002/1.html (citing the key prior art evidence as Rajfer J. et al., *Nitric Oxide as a Mediator of Relaxation of the Corpus Cavernosum in Response to Nonadrenegic, Noncholinergic Neurotransmission*, (1992) 326 NEW ENG. J. MED. 90).

[168] Untold numbers of other drugs have been screened out of development by pharmaceutical companies for reasons related to their patentability, perhaps including drugs for HIV, cancer, heart disease, stroke, diabetes, malaria, tuberculosis, and diarrhea conditions that afflict and kill millions of people each year. Losing an effective treatment for any one of those conditions would be a tragedy, even if it offered only minor improvements in health outcomes.

Benjamin Roin, *Pharmaceutical Innovation and the Limits of the Patent System*, 28-29 (Aug. 31, 2007), *available at* http://www.law.harvard.edu/faculty/workshops/climenko/Roin.pdf.

> protection. This gap in the patent system for drugs has created a pervasive problem in the pharmaceutical industry, causing firms to regularly screen their drugs during the research-and-development process and discard ones with weak patent protection.[169]

Most patent regimes also prohibit the patenting of discoveries, although such discoveries may require significant investments before they are developed and converted into marketable products. The "discovery" exclusion is best captured in a ruling from the U.S.— a WTO member state that is often perceived as one that permits the least derogation from patentable subject matter. Douglas, J., observed, thus, in *Funk Brothers Seed Co. v. Kalo Inoculents Co.:*

> [P]atents cannot issue for the discovery of the phenomena of nature. The qualities of these bacteria, like the heat of the sun, electricity, or the qualities of metals, are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none. He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes. If there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end.[170]

In short, a mere "discovery" cannot constitute an "invention", notwithstanding the fact that truly unique characteristics/properties of a natural substance have been unearthed. At some level, this conclusion derives from the ordinary meaning of the

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[169] *See id.*

[170] *See* Funk Bros Seed Co v. Kalo Inoculant Co. 333 US 127, 131 (1948); 76 USPQ (BNA) 280 (holding that packets containing mixtures of bacteria were "no more than the discovery of some of the handiwork of nature" and were, therefore, not patentable); *see also* O'Reilly v. Morse, 56 US (15 How.) 62 (1853) (holding that abstract principles are not statutory subject matter) *and* Diamond v. Diehr, 450 US 175, 185 (1981) ("[e]xcluded from…patent protection are laws of nature, natural phenomena, and abstract ideas.").

term "invention". While inventions are artificial creations, discoveries are not the result of creation – even if creativity is needed to reveal information concealed in nature.[171]

However, there is much debate around the scope of the "discovery" exclusion and the amount of "artificiality" that is required before something can be resuscitated from the discovery exception and brought into the domain of patentability.[172] Illustratively, in a recent decision involving *Myriad Genetics*, a US district court suggested that isolated DNA sequences are effectively "discoveries" or "products of nature" and, therefore, not patentable.[173]

The challenged patents covered two genes, BRCA1 and BRCA2, which indicate a predisposition towards breast cancer, as well as a diagnostic tool kit using these two genes. American Civil Liberties Union (hereinafter "ACLU"), the patent challenger, claimed that patents were unconstitutional and invalid because "human genes are products of nature, laws of nature and/or natural phenomena, and abstract ideas or basic human knowledge or thought." The ACLU lawsuit in

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[171] *See* Mackay Radio & Telegraph Co Inc. v. Radio Corporation*,* 306 U.S. 86 (1939), ¶ 94 ("While a scientific truth, or the mathematical expression of it, is not [a] patentable invention, a novel and useful structure created with the aid of knowledge of scientific truth may be.") .

[172]*See* Stephen McKenna, *Patentable Discovery,* 33 SAN DIEGO L. REV. 1241 (1996); *see also* Ariel Simon, *Reinventing Discovery: Patent Law's Characterizations of and Interventions Upon Science*, 157 U. PA. L. REV. 2175 (2009); *see also* Michael Risch, *Everything is Patentable,* 75 TENN. LAW REV. 591, 591-658 (2008), *available at* http://works.bepress.com/cgi/viewcontent.cgi?article=1002&context=michael_risch.

[173] *See* Association for Molecular Pathology, et al. v. USPTO, Case 1:09-CV-04515-RW*, available at*, http://www.aclu.org/files/assets/2010-3-29-AMPvUSPTO-Opinion.pdf.

effect, challenged the entire practice of gene patenting.[174] The District Court whilst invalidating the patents held that:

> DNA represents the physical embodiment of biological information, distinct in its essential characteristics from any other chemical found in nature. It is concluded that DNA's existence in an "isolated" form alters neither this fundamental quality of DNA as it exists in the body, nor the information it encodes. Therefore, the patents at issue directed to "isolated DNA" containing sequences found in nature are unsustainable as a matter of law and are deemed unpatentable subject matter under 35 U.S.C. § 101.[175]

However, this decision was overruled by the Court of Appeals for the Federal Circuit[176] which held that the claimed "isolated DNA" defined a distinct chemical entity that lacked covalent bonds to other genetic material and was thus different from the DNA existing in nature.[177] The US Supreme Court vacated the decision of

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[174] *See* Stephen Albainy-Jenei, *ACLU Mob Attacks Breast Cancer Test Patent,* PATENT BARISTAS (May 13, 2009), http://www.patentbaristas.com/archives/2009/05/13/aclu-mob-attacks-breast-cancer-test-patent/.

[175] *See* Association for Molecular Pathology, et al. v. USPTO, Case 1:09-CV-04515-RW, at 3-4, *available at*, http://www.aclu.org/files/assets/2010-3-29-AMPvUSPTO-Opinion.pdf.

[176] *See* Association for Molecular Pathology, et al. v. USPTO and Myriad Genetics Inc., No. 09-CV-4515, at 41-42 (Fed. Cir. July 29, 2011), http://www.cafc.uscourts.gov/images/stories/opinions-orders/10-1406.pdf.

[177] > [I]t is undisputed that Myriad's claimed isolated DNAs exist in a distinctive chemical form—as distinctive chemical molecules—from DNAs in the human body, i.e., native DNA. Native DNA exists in the body as one of forty-six large, contiguous DNA molecules. Each DNA molecule is itself an integral part of a larger structural complex, a chromosome…Isolated DNA, in contrast, is a free-standing portion of a native DNA molecule, frequently a single gene. Isolated DNA has been cleaved (i.e., had covalent bonds in its backbone chemically severed) or synthesized to consist of just a fraction of a naturally occurring DNA molecule….

Association for Molecular Pathology, et al. v. USPTO and Myriad Genetics Inc., No. 09-CV-4515, at 41-42 (Fed. Cir. July 29, 2011), *available at* http://www.cafc.uscourts.gov/images/stories/opinions-orders/10-1406.pdf.

the CAFC[178] in light of its decision in *Mayo Collaborative Services*[179] and remanded the case to the CAFC. The CAFC ruled, again, that "isolated" DNA molecules are not patent-ineligible subject matter.[180]

It is not my intention to define the precise contours of the "discovery" or "product of nature" exclusion in this thesis.[181] Rather, it is to suggest that the discovery exception can potentially exclude many pharmaceutical substances from patentability in a number of jurisdictions, despite the fact that such substances may require risky investments prior to being converted into a marketable drug.

[178] Association for Molecular Pathology v. Myriad Genetics, Inc., 132 S. Ct. 1794 (2012).

[179] Mayo Collaborative Services v. Prometheus, Inc., 132 S. Ct. 1289 (2012).

[180] Association for Molecular Pathology, et al. v. USPTO and Myriad Genetics Inc., No. 09-CV-4515 (Fed. Cir. Aug. 16, 2012), at 7, *available at* http://www.cafc.uscourts.gov/images/stories/opinions-orders/10-1406.pdf.

[181] *See* Prometheus Labs., Inc. v. Mayo Collaborative Servs., 628 F.3d 1347 (Fed. Cir. 2010). The case started in June 2004 when Prometheus sued Mayo in the U.S. District Court, alleging that an announced (but never marketed) Mayo Medical Laboratories diagnostic test infringed two Prometheus patents. Mayo's test measured the same metabolites as Prometheus' test, but Mayo's test used different levels to determine toxicity of the two metabolites. Mayo argued that the Prometheus patents are invalid because they claim subject matter - "natural phenomena" -- that are excluded under patent law. In holding that the claims satisfied § 101, the U.S. Court of Appeals ruling in favour of Prometheus concluded that, in addition to the "administering" step being transformative, the "determining" step was both transformative and central to the purpose of the claims. Specifically, the court held that because the metabolite levels could not be determined by mere inspection, the determining step necessarily required a transformation. The Supreme Court decided against Prometheus on March 20, 2012 holding that Prometheus' process patent is not patent eligible since it incorporates laws of nature. *See* Mayo Collaborative Services v. Prometheus, Inc., 132 S. Ct. 1289 (2012)..

A regime aimed at incentivising the production of new and non-obvious "inventions"[182] is not necessarily suited towards protecting investments underlying an innovative product. Rather, such investments are better protected by preventing the entry of follow-on products into the market, till such time as the investment is recouped along with a rate of return that is commensurate with the "social value" of the innovative product.

This argument is better understood upon contrasting such an investment protection regime with the standard patent regime that provides a uniform rate and range of protection for all inventions, irrespective of their social value and the underlying efforts/investment, a point discussed in detail below.

**2. The Uniformity of a Patent Regime**

Most patent regimes offer a standard twenty year term of protection to all inventions, irrespective of inventive merit, social value or the large investments underlying the invention. This uniform period of protection is mandated by Article 33 of TRIPS.[183]

[182] *See* Hall, *supra* note 3, at 568 (2007) (discussing whether patents do promote innovation at all remains a contestable proposition).

[183] *See* TRIPS, art. 33 ("The term of protection available shall not end before the expiration of a period of twenty years counted from the filing date.").

Some countries have adapted these uniform patent term periods to suit the peculiarities of pharmaceutical innovation, where there is a considerable time lag between the grant of a patent to a pharmaceutical invention and its final development into a drug that is approved for marketing. Some of this lag is attributable to a lengthy regulatory review process.[184] Countries have therefore amended patent regimes to make good the loss of term protection occasioned by such intensive regulatory processes. Popularly known as "patent term extensions", these additional periods of protection are added on to the regular patent protection. In the US pharmaceutical patent term extensions were introduced as part of the 1984 legislative reform package[185] and is equal to the sum of the period of time running from when the drug regulatory application was submitted for approval to the time of approval and half of the clinical trial period (the period of time running from when the drug product was cleared for investigational use).[186] However, the law mandates that the entire patent term extension cannot, in any case, exceed five years. Furthermore, the remaining term of the patent (following FDA approval for the drug) cannot exceed fourteen years.[187]

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[184] *See* J.R. Thomas & W.H. Schacht, *Pharmaceutical Patent Term Extensions: A Brief Explanation*, 2 *available at* http://www.law.umaryland.edu/marshall/crsreports/crsdocuments/RS21129.pdf (last visited Sept. 18, 2011).

[185] *See id*.

[186] *The Hatch-Waxman (Im) Balancing Act*, *available at* http://leda.law.harvard.edu/leda/data/551/Paper1.html (last visited Sept. 18, 2011).

[187] In addition, US Congress on a number of occasions has enacted patent term extensions for specific pharmaceuticals. Thomas & Schacht, *supra* note 184, at 3.

The EU, recognizing the need for similar pharmaceutical patent term extensions, introduced supplemental protection certificates (hereinafter "SPC") for medicinal products.[188] Unlike patent term extensions however, SPCs create a completely new title of intellectual property.[189] The SPC takes effect when the basic patent expires and operates for a duration equal to the period elapsed between the date on which the application for the basic patent was lodged and the date of the first authorization granted to place the product on the market, reduced by a period of five years, and subject to a maximum cap of five years, as in the case of the US.[190]

As evident from the above, patent term extensions merely seek to compensate for delays in procuring regulatory approval. It continues to largely endorse the standard proposition that a fixed patent term period of 20 years is optimal for all drugs, irrespective of the investments incurred in relation to the drug. All that patent term extensions do is to try and ensure that drugs enjoy a term that is close to this 20 year term.

An investment protection regime that compensates for a time period equivalent to the time that it takes to recoup investments in R&D for each individual drug is far more optimal than a uniform period of legal protection.

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[188] *See* Council Regulation (EEC) No. 1978/92 of 18 June 1992.

[189] *See* James Moore, *Patent Term Restoration for Pharmaceutical Products in Europe: The Supplementary Protection Certificate*, *available at* http://www.ipic.ca/reviews/CIPR1413.pdf (last visited: Sept. 18, 2011).

[190] *See id.*

However, it does entail significant administrative costs, an aspect dealt with later in this thesis.

### 3. The Relative Indeterminacy of Patent Standards

I argue that the patentability threshold, most notably the non-obviousness criterion, is relatively indeterminate[191] and ill suited for protecting investments.[192] Apart from this, issues such as claim scope and the applicability or otherwise of the doctrine of equivalents add to the general indeterminacy and uncertainty surrounding the patent regime.[193] All of these have caused some scholars to argue

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191 Some degree of determinacy in the content and application of laws is necessary for individuals to identify the scope of their rights and to ensure that their conduct conforms with legal constraints. In patent law, lack of determinacy has the potential to undermine a fundamental goal of the patent system—providing an incentive for creators to invent and to publicly disclose their inventions. A patent (the incentive) is only as valuable as the laws that give force to it. With an exceedingly uncertain reward, the incentive effect may diminish.

Kelly Casey Mullally, *Legal (Un)certainty, Legal Process, and Patent Law*, 43 LOY. L. A. L. REV 1109, 1135–42 (2010), *available at* http://llr.lls.edu/docs/43-3mullally.pdf; *see also* Lee Petherbridge, *On the Development of Patent Law*, 43 LOY. L. A. L. REV. 893, 907 (2010), *available at* http://llr.lls.edu/docs/43-3petherbridge.pdf (defining the term "legal determinateness" as "capacity of the rules of the law when confronted with a claim to a new invention to conclusively settle patentability—without the need to resort to a costly inquiry into easily disputable factual conclusions.").

192 *See* Bradley G. Lane, *A Proposal to View Patent Claim Non-obviousness From the Policy Perspective of Federal Rule of Civil Procedure 52(a)*, 20 U. MICH. J. L REFORM 1157, 1159 (1987) (noting that obviousness is the most unsettled condition of patent validity, when viewed in terms of quantity of litigation); *see also* Dennis Crouch, *BPAI Review of Obviousness Rejections*, PATENTLYO BLOG (Jan. 19, 2011, 11:30 PM), http://www.patentlyo.com/patent/2010/06/bpai-review-of-obviousness-rejections.html (pointing out that over 85% of the Board of Patent Appeals and Interferences appeals focus on non-obviousness).

193 *See* Alex M. Brill, *Proper Duration of Data Exclusivity for Generic Biologics: A Critique, available at* http://www.tevadc.com/Brill_Exclusivity_in_Biogenerics.pdf (last visited: Sept. 30, 2011) (noting that the inherent uncertainty accompanying patent law, especially with regard to such matters as the application of the doctrine of equivalents, meeting of burdens of proof, "battles of experts,"

that patents cannot be equated with real property, which have more certain and determinate bounds.[194] It is not my intention to explore all areas of indeterminacy in patent law but merely to focus on one of them, namely, the non-obviousness or inventive step criterion with a view to demonstrating that the patent regime is relatively more indeterminate than a comprehensive investment protection regime which protects all drugs that have received regulatory approval, without requiring further thresholds to be met.

At its core, the non-obviousness criterion in patent law asks: would the advancement of the prior art in the manner suggested by the patent applicant have been obvious to a person skilled in the art? This determination is easier said than done, for the distance between the prior art and the claimed invention is a matter of degree and prone to some amount of subjective assessment.[195] This is particularly so in the context of pharmaceutical and biotechnology inventions, where the

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inequitable conduct and more.). For further discussion, see Yaniv Heled, *Patents vs. Statutory Exclusivities in Biological Pharmaceuticals—Do We Really Need Both?*, 18 MICH. TELECOMM. TECH. L. REV. 419 (2012), *available at* http://www.mttlr.org/voleighteen/heled.pdf.

[194] *See* James E. Bessen & Michael J Meurer, *Of Patents and Property* 19 (Boston University School of Law Working Paper No. 09-18), *available at* http://www.bu.edu/law/faculty/scholarship/workingpapers/2009.html (last visited Sept. 21, 2011) (concluding on a review of historical evidence, cross-country studies and economic parameters that in most industries, patents fail to perform like real property); *see also* Michael J. Meurer & Craig Allen Nard, *Patent Policy Adrift in a Sea of Anecdote: A Reply to Lichtman*, 93 GEO. L. J. 2033, 2035 (2005) (noting that, "the standard view in law and economics that fuzzy property rights frustrate investment decisions and impede transactions").

[195] *See* Barton, *supra* note 4 ("The non-obviousness principle….asks whether the invention is an adequate distance beyond or above that state of the art; it clearly and unavoidably, therefore, involves a judgment call."); *see also* Petherbridge, *supra* note 191, at 907 (noting that while the concept of obviousness is simple enough to state, it has proven tremendously difficult to operationalise). Petherbridge states: "[T]he basic policy of obviousness is that advances not apparent to an ordinarily skilled artisan are those that advance human understanding sufficiently to justify the grant of a patent...[t]he measurement cost of obviousness is tremendous."

element of uncertainty is higher than other technological domains.[196] A wide array of cases in the US and other key jurisdictions bear this point out well. Illustratively, consider the *Escitalopram* case involving a patented pharmaceutical enantiomer.[197] While the U.K.[198], German[199], Canadian[200] and Australian courts[201] adjudicated the patent to be a valid one, the Dutch court held that the patent was invalid for obviousness.[202]

Another instance of divergent interpretation of the obviousness criterion is illustrated by the *Viagra* case, discussed earlier in this Chapter.[203] The U.K. courts invalidated the patent on the ground that it was obvious in the light of prior art which suggested the utility of the claimed PDE VA inhibitor in potentially curing erectile dysfunction. However, the Federal Court of Appeal in Canada rejected the above line of reasoning and held that a mere "worth a try" possibility did not

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[196] *See* Timo Minssen, *Meanwhile on The Other Side of The Pond: Why Biopharmaceutical Inventions That Were "Obvious To Try" Still Might Be Non-Obvious – Part I*, 9 CHI.-KENT J. INTELL. PROP. 60 (2010).

[197] *See* Jonathan J. Darrow *The Patentability of Enantiomers: Implications for the Pharmaceutical Industry*, 2007 STAN. TECH. L. REV. 2, (discussing different aspects of enantiomers).

[198] *See* Generics (UK) Limited and others v. H Lundbeck A/S, [2009] UKHL 12.

[199] *See* Lundbeck A/S v. Neolab Ltd. et al. (Escitalopram), invalidity proceedings, Federal Supreme Court, Germany, 10 September 2009, Docket number Xa ZR 130/07.

[200] *See* Apotex v. Lundbeck Canada Inc., 2010 FCA 32.

**[201]** *See* H. Lundbeck A/S v. Alphapharm Pty. Ltd., [2009] FCAFC 70.

[202] *See* Alfred E. Tiefenbacher GmbH s. H. Lundbeck A/S, 312468 / HA ZA 08-1827 (District Court); *see also* Jeremy Phillips, *That (Es)citalopram Patent Again*, THE IPKAT BLOG (Apr. 13, 2009) http://ipkitten.blogspot.com/2009/04/that-escitalopram-patent-again.html (discussing how the Dutch court may have been influenced by the presentation of additional evidence and the presence of Jack Baldwin, a Chemistry expert who did not appear in any of the other trials)

[203] *See* Lilly Icos Llc v Pfizer Ltd., [2002] EWCA Civ 1, *available at* http://www.bailii.org/ew/cases/EWCA/Civ/2002/1.html (last visited Jan. 18, 2011).

preclude inventiveness. Rather, the claimed invention would be obvious, only when the "try" was a matter of routine and required no significant thinking or effort.[204]

The divergent conclusions on obviousness discussed above stem not only from a differential subjective assessment of the same facts,[205] but can also be attributed to a difference in legal standards. As can be seen from the above discussion, Canada preferred a lower non-obviousness or inventive step threshold that would have found in favour of the patentability of a larger number of inventions than the U.K. regime.[206]

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[204] *Compare* Pfizer Canada Inc. v. Apotex Inc. (F.C.A.), 2009 FCA 8, [2009] 4 F.C.R. 223, ¶ 28-31 *available at* http://reports.fja.gc.ca/eng/2009/2009fca8/2009fca8.html (last visited Jan. 18, 2011) (following the standard laid down by the Canadian Supreme Court in an earlier pharmaceutical case, Apotex Inc. v. Sanofi-Synthelabo Canada et al. 2008 SCC 61), *with* Apotex Inc. v. Sanofi-Synthelabo Canada et al. 2008 SCC 61 *available at* http://scc.lexum.umontreal.ca/en/2008/2008scc61/2008scc61.pdf (last visited Jan. 18, 2011) (holding that: "For a finding that an invention was 'obvious to try', there must be evidence to convince a judge on a balance of probabilities that it was more or less self-evident to try to obtain the invention. Mere possibility that something might turn up is not enough.").

[205] The US and other leading patent jurisdictions hold non-obviousness or inventive step to be a question of law, albeit one is that predicated heavily on underlying facts; for e.g., *In re* Kubin, 561 F.3d 1351, 1355 (Fed. Cir. 2009) ("Obviousness is a question of law based on underlying findings of fact."); *see also* Professor Chris Cotropia, *KSR and the Line between Fact and Law*, THE 271 PATENT BLOG (May 6, 2007, 7:38 PM), http://www.patentlyo.com/patent/2007/05/ksr_and_the_lin.html ("Owing to the highly intensive fact specific nature of the enquiry and the subjectivity of the assessment, it is evident that courts may come to differing conclusions on the facts of the same case.").

[206] *See* Pfizer Canada Inc. v. Apotex Inc., 2009 FCA 8, [2009] 4 F.C.R. 223, ¶ 107 (where the court noted: "[t]he test applied by Mr. Justice Laddie appears to be met if the prior art indicates that something may work, and the motivation is such as to make this avenue 'worthwhile' to pursue."); *see also* Sanofi-Synthelabo, *supra* note 204, ¶ 66 (indicating that as such, a solution may be "worthwhile" to pursue even though it is not "obvious to try" or in the words of Rothstein, J., even though it is not "more or less self-evident"). In my view, this approach which is based on the possibility that something might work, was expressly rejected by the Supreme Court in Sanofi-Synthelabo, at ¶66.

It is not my intention to delineate the precise standard for determining the obviousness or otherwise of pharmaceutical inventions. Rather, it is to suggest that the obviousness test suffers from some amount of indeterminacy, both in terms of the legal standard,[207] as also in terms of its application to the facts.[208] A scholar argues that this inherent indeterminacy[209] leads to inefficiently low incentives to research and develop great advances, and excessively high incentives to invest in mundane innovation.[210]

In much the same vein, noted British scholar, William Cornish, argues that the indeterminacy "contributes significantly both to the insecure commercial value

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[207] Harries v. Air King Products, 183 F.2d 158, 162 (2d. Cir. 1950) (per Judge Learned Hand) (characterising the non-obviousness requirement as being "as fugitive, impalpable, wayward and vague a phantom as exists in the whole paraphernalia of legal concepts."); *see also* Lee Petherbridge, *On the Development of Patent Law*, 43 LOY. L. A. L. REV. 893, 905, 907 (2010), http://llr.lls.edu/docs/43-3petherbridge.pdf (stating that: "Justice Woodbury's prediction over 150 years ago" that the law "seems open to great looseness or uncertainty in practice" has largely been validated).

[208] *See* Minssen, *supra* note 196, at 63 (cautioning as to how the highly factual nature of the inquiry leads to unpredictability, uncertainty and arbitrariness). Minssen argues:

> The evaluative nature of the inquiry also implies that reasonable people, including judges, juries, patent examiners, or even the rather mystical imaginary persons skilled in the art, can easily reach different conclusions at different times, thus making it extremely difficult to foretell the result of an obviousness attack or objection. This unpredictability has led to the arbitrary use of discretion and to accusations of uncertainty.

[209] *See* Gregory N. Mandel, *The Non-Obvious Problem: How the indeterminate Non-Obvious Standard Produces Excess Patent Grants,* 42 U. C. DAVIS L. REV. 57 (2008) (discussing the indeterminacy of the non-obviousness standard in patent law)He notes:

> [T]he dominant current perception in patent law is that the core requirement of non obviousness is applied too leniently, resulting in a proliferation of patents on trivial inventions that actually retard technological innovation in the long run. This Article reveals that the common wisdom is only half correct. The non-obviousness standard is not too low, but both too high and too low. It is indeterminate.

[210] *See id.* at 60.

of many patents and to the cost of litigating their validity."[211]If high risk and large investments are the key reasons for desiring legal protection from free riders, it makes better sense to protect such investments directly, rather than shoehorning them into the inventive step criterion, which has largely been framed as a "cognitive" enquiry.[212]

An explicit investment protection regime that grants legal protection commensurate with the level of investment, such that the investor is able to ward off free-riders until such time as she recovers the investment and makes an appropriate rate of return depending on the health value of the product is likely to be a more determinate legal instrument than the current patent regime.[213] This thesis advocates such a comprehensive investment protection regime.

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[211] *See* William Cornish, *The Essential Criteria for Patentability*, 14 IIC 765, 771 (1983); *see also* FRITZ MACHLUP, SUBCOMM. ON PATENTS, TRADEMARKS & COPYRIGHTS OF THE COMM. ON THE JUDICIARY, AN ECONOMIC REVIEW OF THE PATENT SYSTEM, 85TH CONG., 2D SESS. (Comm. Print 1958) (describing the shortcomings of patents). Machlup argues:

> The patent system lacks logic. It postulates something called 'invention' but in fact no satisfactory definition of "invention" has even appeared, and the courts, in their search for guiding rules, have produced an almost incredible tangle of conflicting doctrines. This confusion has led to extensive and costly litigation. Its critics have described the patent right as "a lottery in which it is hardly worthwhile taking out a ticket."..... It is almost impossible to conceive of any existing social institution so faulty in so many ways. It survives only because there seems to be nothing better.

[212] *See* Michael Abramowicz & John Duffy*, The Inducement Standard of Patentability,* 120 YALE L. J. 1590, 1592 (2011) (arguing that the inventive step test has largely been interpreted through a cognitive lens, focusing on whether individuals have epistemic awareness of technological solutions to problems).

[213] Mullaly, *supra* note 191, at 1113 (discussing the uncertainties faced by patentees under the patent system). He notes:

> Patentees may be unable to ascertain their rights and obligations without engaging in costly litigation. They also may be unable to obtain the financing necessary to bring their innovations to market in the form of a commercial product when their

### D. The Risk of Diluting Patentability Criteria

As mentioned earlier, any attempt to shoehorn an investment-based rationale into the existing patent framework is likely to lead to a lowering of the patentability threshold. Illustratively, Merges advocates a "moderate lowering of patentability standards for very high cost research."[214] Similarly, another reputed law and economics scholar, Suzanne Scotchmer suggests that, "it is not inconceivable that patent offices could consider costs in their interpretation of non-obviousness" while granting patents.[215]

Most tellingly, Judge Rader of the Court of Appeals for the Federal Circuit in the U.S. notes:

> Many if not most pharmaceutical inventions are discovered through a routine screening protocol or through an established trial and error process. Pharmaceutical inventions discovered by these routine-screening methods include not only new formulations and salt forms, but also include the active pharmaceutical compounds themselves. Thus, this decision calls into question countless pharmaceutical patents, which in turn could have a profoundly negative effect on

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> patent rights are uncertain. Knowing these possibilities, inventors may be deterred from entering the patent system and even discouraged in their creative efforts.

[214] *See* Robert P. Merges*, Uncertainty and the Standard of Patentability,* BERK. TECH. L. J. (1993), http://www.btlj.org/data/articles/vol7/Merges.pdf.

[215] *See* Suzzane Scotchmer, *Patent Quality, Patent Design, and Patent Politics*, 10 (Dec. 10, 2004), *available at* http://socrates.berkeley.edu/~scotch/Scotchmer_epo.pdf . ("[t]he mere recognition that costs should matter to the size of the reward gives some guidance as to how intellectual property law should be structured.").

> investments into the design and development of new life-saving pharmaceuticals.[216]

I question this misconceived sentiment.[217] If investment protection is the goal, current patent law and doctrine are ill-suited for achieving it. Lowering the novelty and inventive step threshold in order to protect pure investments into R&Dwould dilute the very essence of the patent regime, namely the protection of new and inventive ideas, which have been reduced to practice in some form.[218]

In the context of copyright law, a scholar has argued that while the US copyright regime protects a wide range of works, it is susceptible to interpretative flexibility, such that courts might draw distinctions between different kind of

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[216] Illustratively, see Pfizer Inc. v Apotex, 488 F.3d 1377; 2007 U.S. App. LEXIS 11886; 82 U.S.P.Q.2D (BNA) 1852 (Rader, J.,); *see also* Teva Pharmaceutical Industries Ltd. and others v. Istituto Gentili SpA and Merck & Co. Inc., [2003] EWHC 5 (Pat), where Jacob, J., invalided two of Merck's U.K. alendronate "use" patents with some remorse and noted:

> I accordingly hold both patents invalid. I do so with some regret. Merck have only had a few years' exclusive exploitation of alendronate. They must surely have had to make a very considerable investment and incurred considerable risk in bringing it to market. And mankind is better off as a result. But the patent system does not confer monopolies on those who develop obvious or old products, even if they have never been exploited. A workable system for that might be a good idea, particularly in the field of medicines and analogous fields.

[217] Some judicial decisions have alluded to the proposition that expensive experimentation tends to infuse a hue of "inventiveness" to the alleged invention. *See, e.g.,* Edoco Technical Products, Inc. v. Peter Kiewet Sons' Co. 313 F. Supp. 1081 (1970) (the district court upheld the inventiveness of the invention on the ground that "a long and expensive period of experimentation was required by the patentees to solve the problem . . . .").

[218] *See* Sichelman, *supra* note 98, at 345 (stating that a traditional patent system is "designed to spur the *creation* of new and non-obvious *knowledge*"); *see also* W. R. CORNISH, INTELLECTUAL PROPERTY: PATENTS, COPYRIGHT, TRADE MARKS AND ALLIED RIGHTS 54 (4th ed. 1999); *see also* Brenner v. Manson, 383 U.S. 519, 534–35 (1966) (requiring that a claimed invention must meet specific and substantial practical utility standards); 35 U.S.C. §§ 101, 112 (requiring that an invention be "new and useful" and that "[t]he specification shall contain . . . the manner and process of making and using it").

creative works and provide greater protection for more creative works.[219] While this is no doubt true (particularly for common law countries), one must also be cautious of the risk inherent in unbridled interpretative flexibility, where the copyright or patent protection pre-requisite is interpreted in so lax a manner that it effectively whittles away the essence of the pre-requisite itself.

This brings to mind the classic Aristotelian distinction between essence/kind on the one hand, and attributes/quality on the other.[220] The inventive step filter lies at the heart of patent philosophy and it may in many ways, constitute its essence.[221] If this were to wither away, it would be disingenuous to pretend that one continues to work within the bounds of a patent regime. Secondly, a dilution of the inventive step threshold would also aid the process of ever-greening, a phenomenon that is widely criticised across countries and discussed at length in a later chapter.

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[219] *See* Shyamkrishna Balganesh, *TIERED ORIGINALITY AND THE DUALISM OF COPYRIGHT INCENTIVES*, 95 VA. L. REV. IN BRIEF 67, 75-76 (2009) ("One could imagine a sliding scale of creativity—along the lines that Parchomovsky and Stein propose—coupled with a rule that alters what is considered "copying" based on where on the spectrum a particular work's creative contribution lies. Works of exceptional creativity would have a broader entitlement, perhaps extending to the "total concept and feel" test for substantial similarity, while those of average creativity would have a shorter leash, and those of very low originality would be relegated to having to show "virtually identical copying" for infringement to lie." (footnotes omitted)).

[220] *See* David Vaver*, Invention in Patent Law: A Review and a Modest Proposal,* 11(3) INTL. J. LAW AND IT 287 (2003) (cautioning, however, in a footnote that: "the distinction between kind and quality cannot be pressed too far; for e.g., one might fairly argue that novelty and non-obviousness are part of an invention's essence.").

[221] *See* Giles S. Rich, *Non-obviousness--the Ultimate Condition of Patentability,* paper prepared for the Bureau of National Affairs, Inc. at §1:201-1:213 (John F. Witherspoon ed. 1980) (stating that non-obviousness is "the ultimate condition of patentability"); *see also* ROBERT MERGES & JOHN DUFFY, PATENT LAW AND POLICY, 612 (4th ed. 2007) (categorising the non-obvious requirement as the "final gatekeeper").

A recent paper by Michael Abramowicz and John Duffy also appears to advocate a dilution of the inventive step or non-obviousness threshold. The authors argue that the rationale underlying the inventive step criterion ought to shift from the prevalent "cognitive" theory to a more explicit economic one.[222] Towards this end, they advocate the use of an "inducement" standard, wherein the key enquiry is: would the invention have emerged in a timely fashion without the inducement of a patent regime?[223] They note that the "time factor" is important, since almost all inventions are likely to emerge at some point in time, even absent a patent system.[224]

Their approach castigates the oft-used "cognitive" approach in determining inventive step, as one that is indeterminate.[225] They argue that an economic "inducement" standard comports better with the purpose and function of the patent system and that it finds jurisprudential support in the epochal case, *Graham v. John Deere Co.*[226] where the Supreme Court called for "weeding out those

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[222] *See* Abramowicz & Duffy, *supra* note 212.

[223] In many ways, this line of argument is similar to what Kitch had proposed several decades ago. Edmund W. Kitch*, Graham v. John Deere: New Standards for Patents*, 1966 SUP. CT. REV. 293, 301 (stating that, "a patent should not be granted for an innovation unless the innovation would have been unlikely to have been developed absent the protection of a patent."); *see also* S. C. Gilfillan, *The Root of Patents, or Squaring Patents by their Roots*, 31 J. PAT. OFF. SOC'Y 611, 611 (1949) ("A patent is helpful and proper when it rewards sufficiently useful creative work which might not have been done without that prospective reward. . . .").

[224]*See generally* Abramowicz & Duffy, *supra* note 212.

[225] *See id*. at 1596.

[226] *See* Graham v. John Deere Co., 383 U.S. 1, 11 (1966).

inventions which would not be disclosed or devised but for the inducement of a patent."

While the "inducement" theory attempts to resolve a long-standing doctrinal inconsistency with the non-obviousness enquiry (where although the standard speaks of a "cognitive" enquiry, economic considerations have slipped in without explicit acknowledgement), one is not certain that their test would necessarily be susceptible to a more determinate application. For, how is one to determine whether the absence of a patent regime would have yielded the invention in question? Any honest answer is likely to border on the speculative. Innovation is about risk and uncertainty and even the best of wizards find it impossible to accurately predict what inventions are likely to emerge in future, and whether such inventions will convert successfully into marketable products.[227]

But first, it is important to ask whether or not patents foster accelerated rates of innovation. Abromowicz and Duffy make a positive assumption in this regard in favour of patents and set about deploying patent doctrine to locate those cases of accelerated innovation as ones that deserve protection. One might see this frame of enquiry as nothing more than begging the question. As has already been demonstrated, the very notion that patents spur accelerated innovation is itself under doubt. A large number of scholars have pointed to non-patent incentives

[227] *See* Sichelman, *supra* note 98, at 343.

such as lead-time and trade secrecy as being more effective incentives that spur innovative products in several cases.[228]

Based on this lack of empirical evidence supporting the theory that patents necessarily induce accelerated innovation, one might argue that on a proper application of the Abromowicz and Duffy's inducement test, the patentability of many an invention would be thrown into doubt, particularly inventions in fields such as software and electronics, which are often hailed as technology sectors where innovation was likely to flourish without patents, perhaps even better so.[229]

However, their test is likely to support the grant of patents for high risk and high investment industries such as pharmaceuticals.[230] If high risk and intensive investments are the key triggers for desiring legal protection from free-riders, I argue that it would make better sense to protect such investments directly, rather than shoe-horning them into the inventive step criterion.

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[228] *See* Wendy H. Schacht*, Patent Reform: Issues in Biomedical and Software Industries* (2007), available at http://www.ipmall.info/hosted_resources/crs/RL33367_070507.pdf. ("In computer and semi-conductor industries firms rely heavily on secrecy, lead time and complementary capabilities to protect their inventions…. not so much in pharmaceutical industry which according to the author is more dependent on patent protection."); *see also* Ashish Arora*, Patents, Licensing and Market Structures in Chemical Industry,* 26 RESEARCH POLICY 391 (1997) (explaining how chemical firms at times protect an innovation by applying for multiple patents on different elements of the innovation while keeping some others a secret).

[229] *See* Graham et al., *supra* note 87; *see also* Hall *supra* note 3.

[230] *See* Abramowicz & Duffy, *supra* note 212, 1599 ("The pharmaceutical industry provides a stark contrast because it is known to depend heavily on patent incentives to fund its research.").

The investment protection regime advocated by this thesis bears some resemblance to existing "data protection" regimes,[231] which protect investments incurred in the course of generating regulatory data i.e. "safety" and "efficacy" data that are required to be submitted to a drug regulatory authority to procure marketing approval.[232] This data generation from the various clinical trials accounts for a major part of drug discovery and development costs.[233] The next Chapter discusses and critically assesses the data exclusivity regime and its suitability as a comprehensive investment protection instrument.

## E. Overview of Discussion

Based on the limited empirical evidence generated to date, it would appear that patents play a very limited role in fostering innovation. Any prospects of incentivising innovation ought to be weighed against the "costs" of operating the patent regime (costs to patent applicants, competitors and the government) and the "social" costs of the system in general, whereby patents potentially stymie the

[231] These include the United States, European Union and Japan. The list is constantly increasing due to provisions in various Free Trade Agreements (FTA's) that mandate data exclusivity. Illustratively, see Carsten Fink & Patrick Reichenmiller, *Tightening TRIPS: Intellectual Property Provisions of U.S. Free Trade Agreements in* TRADE, DOHA AND DEVELOPMENT 289-303 (Newfarmer ed. 2006).

[232] *See generally* Mossinghoff, *supra* note 5; *see also* Heller and Eisenberg, *supra* note 92.

[233] *See* DiMasi et al., *supra* note 6, at 165.

downstream development of technology,[234] reduce levels of competition and cause deadweight losses.[235] Seen in this light, the case for a patent system is rather weak.

Scholars however treat the pharmaceutical industry as an exception, noting that the high costs endemic to the industry warrants the institution of a patent regime to protect such drugs from free riders. I take issue with this line of thinking, arguing instead that if the purpose is to simply enhance levels of investments in pharmaceutical R&D; such a purpose is better served by a comprehensive investment regime that protects investments from free riders, rather than patents. Patents suffer a number of drawbacks in this regard. For one, they protect only those inventions that satisfy certain thresholds such as novelty and inventive step, without regard to the fact that even known non-patentable substances require tremendous developmental costs. Secondly, the patent regime is relatively indeterminate, particularly since it is premised on patentability thresholds such as the "inventive step" which require a highly subjective assessment.

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234 Ultimately it is important to bear in mind that every potential inventor is also a potential infringer. Thus, a "strengthening" of property rights will not always increase incentives to invent; it may do so for some pioneers, but it will also greatly increase an improver's chances of becoming enmeshed in litigation. Indeed this is the very heart of our case.

Merges & Nelson, *supra* note 91, at 916.

235 *See* Jay P. Kesan & Marc Banik, *Patents as Incomplete Contracts: Aligning Incentives for R&D Investment with Incentives to Disclose Prior Art,* 2 WASH. U. J.L. & POL'Y 23, 24 (2000) ("Patents also impose social costs such as reduced levels of competition or wasteful design-around efforts by competitors. Thus, efficient patent systems aim to induce investment in R&D while limiting losses due to market power.").

Thirdly, patents are granted to all new inventions for a uniform term without regard to the "value" of the invention and the amount of costs incurred in discovering the invention or developing it. Lastly, I caution that any attempt to adapt the patent regime to a full-fledged investment protection regime would destroy its core essence, which is that of protecting new and non-obvious inventions.

In short, it is far more optimal to institute a comprehensive investment protection regime for fostering higher levels of investment into pharmaceutical R&D. One might argue that a determination of the kinds of investment that are to merit protection and the baseline for such protection will prove difficult. While this may hold true within a general innovation context, it is more amenable to an objective determination within the pharmaceutical technology sector, where drugs are subject to a rigorous regulatory framework and cannot be marketed until approved.[236] Therefore, any costs associated with drug discovery and development beginning with the identification of the target until final drug approval ought to be covered and compensated for.

[236] *See* Eisenberg, *supra* note 20.

## CH III. DATA EXCLUSIVITY AND PHARMACEUTICAL INNOVATION

A number of countries protect the significant investments underlying clinical trial data by stipulating that data submitted by a drug originator to gain marketing approval cannot be relied upon by the drug regulator to approve any other drug for a certain period of time.[237] This effectively creates a period of market exclusivity for drug originators and is commonly referred to as "data exclusivity". The below sections discuss the current data exclusivity regimes in the US and EU.

### A. Overview of Data Exclusivity Regime

Regulatory norms the world over stipulate that no new drug can be introduced in the market without the approval of the drug regulator. Illustratively, in the US, firms are required to file a new drug application (hereinafter "NDA") before the drug regulator (FDA)[238] and submit extensive clinical trial and other data to demonstrate the safety and efficacy of their drug.[239] However, the process for approving a generic is far less complex, with an applicant having to simply file an

[237] *See* International Federation of Pharmaceutical Manufacturers Association, *A Review of Existing Data Exclusivity Legislation in Selected Countries* (2005), *available at* http://www.ifpma.org/documents/NR2799/DataExclusivity_2005.pdf (noting that U.S., EU, Australia, New Zealand and Israel currently provide for data exclusivity).

[238] *See* 21 U.S.C. § 355(a)

[239] *See* 21 U.S.C. § 355(b)

Abbreviated New Drug Application (hereinafter "ANDA") that demonstrates their generic version to be bio-equivalent to the existing originator drug.[240]

Proof of bio-equivalence, which largely hinges on a demonstration of equivalent bioavailability,[241] obviates the need to undertake fresh clinical trials by the generic applicant. The underlying rationale is that if the active ingredient is the same, the trial results for the originator drug (demonstrating that the drug is safe and effective) ought to hold good for the generic version as well. Consequently, a generic manufacturer can free-ride on the efforts of the originator and introduce a follow-on drug into the market by expending far less resources than the drug originator.

In order to prevent such free-riding, some legal regimes mandate that the data submitted by an originator cannot be relied upon to approve any generic version for a certain minimum number of years. The extent and length of protection varies between the different countries and depends, in part, on the kind of drug/indication sought to be approved. Illustratively, the U.S. and EU positions are set out below:

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[240] *See* 21 U.S.C. § 355(j) (providing that in the United States, such an application by the generic company is referred to as an Abbreviated New Drug Application or ANDA.)

[241] *See* 21 CFR Section 320.1(a)) ("Bioavailability means 'the rate and extent to which the active drug ingredient or active moiety is absorbed from a drug product and becomes available at the site of drug action.'").

## 1. US Position

**(i) New Chemical Entity Exclusivity:** Drugs based on new chemical entities (hereafter "NCE")[242] are entitled to an exclusivity period of 5 years.[243] However, given that an ANDA cannot be filed during this 5 year period and it can take several months for the said ANDA to gain approval, the period of exclusivity is often longer than five years.[244] This is a feature unique to an NCE, since in other cases, it is the approval of an ANDA which is prohibited during the exclusivity period, and not its filing.[245]

**(ii) New Uses/Indications of existing drugs:** This category includes any application for an existing drug (containing a previously approved active ingredient), for which a new use or indication has been discovered. Upon the

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[242] *See* U.S. FDA, *Small Business Assistance: Frequently asked questions for New Drug Product Exclusivity*, http://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm069962.htm. (last visited Sept. 30, 2011) (noting that a new chemical entity means a drug which contains no active moiety that has been approved by the FDA in any other application).

[243] *See* Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 355(j)(5)(F)(ii); *see* generally, Elizabeth H. Dickinson, *FDA's Role in Making Exclusivity Determinations,* 54(2) FOOD & DRUG L. J. 195 (1999); *see also* Mossinghoff, *supra* note 5.

[244] However, it bears noting that an ANDA application may be submitted after four years, if the application contains a certification that a patent covering the drug in question and listed in the Orange book is either invalid or not infringed. If the ANDA applicant succeeds in this patent challenge, it acquires six month exclusivity in the market. This exclusivity is intended as an incentive for the first generic applicant to challenge a listed patent for the innovator drug product. Dickinson, *supra* note 243, at 199-200.

[245] *See id.* at 200.

generation of clinical trial data pointing to such new uses, new dosages or new indications, the said drug is entitled to 3 years of data exclusivity.[246]

**(iii) Orphan drug exclusivity:** A period of exclusivity lasting up to 7 years is granted to approved orphan drugs, defined under the Orphan Drug Act, 1983 (hereinafter "ODA") as products that treat rare diseases and conditions affecting less than 200,000 patients in the country.[247] The rationale behind such enhanced exclusivity is to encourage R&D in orphan drugs, a category traditionally neglected by large pharmaceutical firms. ODA driven exclusivities have been widely hailed as a success, and a number of new orphan drugs have emerged since the inception of the ODA.[248]

Apart from the time period of protection, ODA exclusivity differs from conventional data exclusivity in another important respect. While the latter merely protects the clinical trial data, the former provides complete market exclusivity for such period, thereby preventing a competitor from entering the market, even if it

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[246] *See id.* at 201.

[247] *See* M. Angeles Villarreal, *Orphan Drug Act: Background and Proposal Legislation in the 107th Congress* (July 25, 2001), *available at* http://www.law.umaryland.edu/marshall/crsreports/crsdocuments/RS20971.pdf (noting that it is estimated that approximately 25 million people in the US suffer from an estimated 6,000 rare diseases and conditions termed as 'orphan' diseases, since these are often neglected by the pharmaceutical industry owing to their potentially small markets and low return on investment).

[248] *See* Marlene E. Haffner, *Adopting Orphan Drugs – Two Dozen Years of treating Rare Diseases,* 354(5) NEW ENG. J. MED. 445 (2006) (noting that in 24 years after the passing of the law, 282 drugs for the treatment of such disorders were brought to the market, as compared to just 10 drugs in the 8 to 10 years before the passing of the law); *see also* Aaron S. Kesselheim, *Using Market-Exclusivity Incentives to Promote Pharmaceutical Innovation*, 363 NEW ENG. J. MED. 1855 (2010).

were able to generate its own data.[249] In other words, in all conventional cases of data exclusivity (NCE and new uses/indications), a generic competitor could potentially conduct its own tests, generate data, procure approval and enter the market immediately after the originator. However, the market exclusivity granted under the ODA is much stronger and precludes this possibility.

**(iv) Paediatric exclusivity:** This exclusivity is granted to encourage trials on paediatric populations.[250] Paediatric exclusivity is unique in that it is not a stand-alone exclusivity protection, but attaches itself as an additional period to already existing periods of exclusivity that the drug is entitled to. Therefore, if the innovator drug is protected at that point in time by a 5 year NCE exclusivity, submission of paediatric studies would extend that exclusivity by another 6 months.[251] Further, if the drug is covered by a patent, a 6 months' data exclusivity period is added on from the date that the patent expires.[252]

The above rules pertain to conventional pharmaceutical drugs,[253] where the equivalence between the chemical composition of an innovator and a generic drug

[249] *See* Eisenberg, *supra* note 20, at 359-61.

[250] *See* The Food and Drug Administration Modernization Act Pub. L. No. P.L. 105-115, 111 Stat. 2296 (21 U.S.C. 301) (1997); *see also* Dickinson, *supra* note 243, at 203.

[251] *See* 21 U.S.C. § 111(1997).

[252] *See id*.

[253] Conventional drugs are small molecule drugs produced by chemical processes. Rader, *supra* note 17; *see also* Linfong Tzeng, *Follow-On Biologics, Data Exclusivity and the FDA*, 25 BERK. TECH. L. J. 135, 136 (2010).

is relatively easy to establish. However, in so far as biologics[254] are concerned, there continues to be considerable uncertainty about whether or not a mere demonstration of structural equivalence would suffice to demonstrate "sameness" in efficacy and toxicity. This is owing to the fact that biologics are much larger in size and more complex in structure that conventional chemical molecules[255] and a small change in the process of manufacture could change properties to a significant extent.[256] It is important to note that the Hatch-Waxman Act, 1984 which provides for an abbreviated regulatory pathway for generics based on a demonstration of bio-equivalence, applies only to conventional small molecule drugs and not to biologics.[257]

**2. EU Position**

[254] *See* Rader, *supra* note 17.

[255] *See* Judith A. Johnson, *FDA Regulation of Follow-On Biologics* (Apr. 26, 2010), *available at* http://www.primaryimmune.org/advocacy_center/pdfs/health_care_reform/Biosimilars_Congressional_Research_Service_Report.pdf.

[256] *See* Maxwell R. Morgan, *Regulation of Innovation under Follow-on Biologics Legislation: FDA Exclusivity as an Efficient Incentive Mechanism*, XI COLUM. SC. & TECH. L. REV. 93, 96 (2010); *see also* David M. Dudzinski, *Reflections on Historical, Scientific, and Legal Issues Relevant to Designing Approval Pathways for Generic Versions of Recombinant Protein – Based Therapeutics and Monoclonal Antibodies,* 60 FOOD & DRUG L. J. 143, 196-7 (2005); *see also* Andrew M. Wasson, *Taking Biologics for Granted? Takings, Trade Secrets and Off-Patent Biological Products*, 2005 DUKE L. & TECH. REV. 4, 10 (2005), *available at* http://www.law.duke.edu/journals/dltr/articles/pdf/2005dltr0004.pdf.

[256] *See* Tzeng, *supra* note 253, at 141.

[257] *See* Tzeng, *supra* note 253, at 141.

Much like the US, the EU also mandates that all drugs must gain regulatory approval prior to being placed on the market.[258] Market authorisations can be obtained in two ways:

(i) Community Authorisations, issued by the European Medicines Agency (hereinafter "EMEA") which extends to all EU markets; and

(ii) National Authorisations, issued by the relevant authorities in each of the member states and covering their respective territories, unless extended to other member states via a mutual recognition procedure (MRP).[259]

Data exclusivity is enforced through a regime similar to that of the U.S., i.e. by disallowing "generic" applicants to file abbreviated applications (demonstrating bioequivalence to previously approved drugs), until a certain number of years have expired. However, the time period of protection varies and is encapsulated by what is commonly referred to as the 8+2+1 rule:

i) Abridged applications (by follow-on competitors) can be filed only after 8 years have elapsed from the date of approval of the reference product.

ii) Abridged applications cannot be approved until at least 10 years have elapsed from the approval of the reference product.[260]

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[258] *See* European Commission, *Pharmaceutical Sector Inquiry: Preliminary Report* (DG Competition Staff Working Paper, Nov. 28, 2008), *available at* http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/preliminary_report.pdf.

[259] *See id.* at 103.

[260] *See* European Commission, Directive 2004/27/EC, art. 10.1.

iii) The above period is extendable by another year if a new therapeutic indication with significant clinical benefits is found.[261]

## B. Biologics and Data Exclusivity

The above rules pertain to conventional pharmaceutical drugs,[262] where the equivalence between the chemical composition of an originator drug and its generic version is relatively easy to determine. However, in so far as biologics[263] are concerned, there continues to be considerable uncertainty about whether or not a mere demonstration of bio-equivalence suffices to demonstrate "sameness" in efficacy and toxicity. For, biologics are larger in size and more complex in structure that conventional chemical molecules[264] and a small change in process of manufacture could change the properties to a significant extent.[265] As noted earlier, the Hatch-Waxman Act, 1884 which provides for an abbreviated regulatory pathway for generics based on a demonstration of bio-equivalence, applies only to conventional small molecule drugs and not to biologics.[266]

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[261] *See* European Commission, *surpa* note 258, at 90.

[262] Conventional drugs are small molecule drugs produced by chemical processes. Rader*, supra* note 16; *see also* Tzeng, *supra* note 253, 136.

[263] *See* Rader*, supra* note 17.

[264] *See* Johnson, *supra* note 255.

[265] *See* Morgan *supra* note 256; . Dudzinski,*supra* note 256; Wasson, *supra* note 256.[265] *See* Tzeng, *supra* note 253, at 141.

[266] *See id*.

After much debate and considerable lobbying in the U.S., the Public Health Services Act, 1944 which deals with biologics was amended to provide an abbreviated regulatory pathway for follow-on biologics that were "highly similar" to the reference product.[267] Under this new regime, a follow-on entrant has to demonstrate close similarity to an approved biologic product and establish purity, safety and efficacy through clinical or laboratory based studies.[268] The new law also provides that the reference product is entitled to 12 years of data exclusivity, a substantially longer period than the 5 years available for conventional pharmaceutical drugs under the Hatch-Waxman Act.[269]

As for the EU, it appears to have resolved this issue prior to the US by providing in its 2004 Directive[270] for abridged authorisations of biological medicinal products that are "similar" to the reference product.[271] However, the length of data exclusivity is the same as that provided for small molecule conventional drugs.

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[267] The Patient Protection and Affordable Care Act contains within its fold a sub-section titled the 'Biologics Price Competition and Innovation Act' [hereinafter BPCI Act]. The BPCI in turn amends the Public Health Services Act to provide for abbreviated pathway for biologics. *See* 42 U.S.C. § 262(k)(2)(A)(i)(I); *see also Approval Pathway for Biosimilar and Interchangeable Biological Products Public Hearing; Request for Comments*, 75 Fed. Reg. 61497 (October 5, 2010), *available at* http://www.federalregister.gov/articles/2010/10/05/2010-24853/approval-pathway-for-biosimilar-and-interchangeable-biological-products-public-hearing-request-for#p-10.

[268] *See* Amber W. Aagaard et al., *Review, Approval and Marketing of Biosimilars in the United States*, BIO PROCESS INTERNATIONAL (2010), http://www.bioprocessintl.com/multimedia/archive/00111/BPI_A_100811AR02_O_111127a.pdf.

[269] *See* 42 U.S.C. 262(k)(7)(A)

[270] In Sandoz GmbH v. Commission, T-105/04, the Commission, despite a positive opinion from the EMEA, refused to grant an authorisation to Sandoz for their Omnitrop product. Sandoz's challenge to the Commission's decision however was dropped once the new regime came in. For an interesting discussion on this point, see TREVOR COOK, PHARMACEUTICALS BIOTECHNOLOGY AND THE LAW 474 (2009).

[271] *See* European Commission, *supra* note 260, at art. 10.4; *see also* COOK, *supra* note 270, at 474-7.

### C. Data Exclusivity and Innovation

Emerging as they do out of a regulatory framework aimed at producing safe and effective drugs, data exclusivity norms share a unique position in the pharmaceutical innovation matrix. Essentially, they compensate a drug originator for the costs associated with the generation of clinical trial data i.e. data that is critical to a determination of the safety and efficacy of a drug. But for such protection, data may never have been generated, owing to fears of free-riding by generic manufacturers who could enter the market at a significantly cheaper cost by merely relying on the expensive data already generated by drug originators.[272] Legal incentives for data generation, therefore, aid the regulatory process and promote the overall goal of consumer protection. However, such legal incentives also play a significant role in pharmaceutical innovation, as they aid the production of new innovative drugs.[273]

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[272] See Eisenberg, *supra* note 20, at 372-373, 388 (commenting on the FDA's core function). She states:

> [T]he FDA's core function of reviewing data from clinical trials to determine the safety and efficacy of drugs prior to market approval may be understood as a means of promoting costly investments in a particular form of R&D, rather than simply as a means of protecting patients from untoward risks of harm.

[273] A commentator challenges the central argument that drug regulation and drug innovation are necessarily at odds with one another. He argues that, "[A]lthough intuitively appealing, the argument that drug regulation negatively affects the incentives to innovate does not fully capture the role that regulation plays in this industry." He also argues that drug regulation provides certification of drug quality. Therefore, rather than decreasing the expected returns to innovation, this aspect of regulation contributes to the value of new drugs and may actually encourage innovation. For a discussion on this point see Ariel Katz, *Pharmaceutical Lemons: Innovation and Regulation in the Drug Industry*, 14 MICH. TELECOMM. TECH. L. REV. 1 (2007).

It is logical to assume that the level of investment made by a drug originator is likely to be dependent on the extent of protection granted against free-riders. In an article widely regarded as a classic in the literature on patents and innovation, Merges and Nelson note:

> Although there are still a great many unanswered questions in this field, the following general points seem to be widely accepted: First, increases in research and development expenditures yield more inventions. Second, the larger numbers of inventions from increased research and development have a positive effect on future productivity growth. And third, productivity growth is important for economic well-being.[274]

Some scholars suggest that this common sensical wisdom has been endorsed by the success of the ODA, a regime which, as noted earlier, aims at incentivising clinical trials and developmental work in relation to neglected orphan drugs by providing a 7 year market exclusivity period, during which time no follow-on entrant can even apply for marketing approval.[275] It is estimated that after the enactment of the ODA, 352 orphan drugs were approved in the U.S.,[276] with the rate of approvals

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[274] *See* Merges & Nelson, *supra* note 91, at 871, 878 (citing Griliches, *Introduction*, in R & D, PATENTS, AND PRODUCTIVITY 1, 17 (Z. Griliches ed. 1984); Pakes & Griliches, *Patents and R & D at the Firm Level: A First Look*, *in* R & D, PATENTS & PRODUCTIVITY 55)).

[275] *See* Richard A. Merril, *The Architecture of Government Regulation of Medical Products*, 82 VA. L. REV. 1753, 1791 (1996) ("[t]here is a general agreement that the Orphan Drug Act produced the economic incentives needed to promote drug development of drugs for rare diseases."); *see also* Mark Shtilerman, *Pharmaceutical Inventions: A proposal for Risk-Sensitive Rewards*, 46 IDEA 337, 342 (2006); *contra* Patricia J. Kenney, *The Orphan Drug Act--Is it a Barrier to Innovation? Does it Create Unintended Windfalls?,* 43 FOOD DRUG COSM. L. J. 667 (1988); *see also* David D. Rohde, *The Orphan Drug Act: An Engine of Innovation at What Cost?*, 55 FOOD DRUG COSM. L. J. 125, 134 (2000).

[276] This figure takes into account both the List of Orphan Drug Approvals as well as the Drugs@FDA database and holds good up to May 2009. Olivier Wellman-Labadie & Youwen Zhou, *The US Orphan Drug Act: Rare Disease Research Stimulator or Commercial Opportunity?,* 95 HEALTH POLICY 216, 219 (2010), http://www.floegel.info/Regulatory_OrphanDrug/ORPHAN_WellmanLabadie2010%20US%20Orph

increasing each year. [277]

When compared with the patent regime, the data exclusivity regime seems better suited for protecting investments in pharmaceutical R&D. For one, a data exclusivity regime is relatively more determinate than existing patent regimes. Upon successful FDA or other regulatory approval, the drug in question is automatically entitled to an exclusivity period. The only issue for determination then is the type of exclusivity that the drug is entitled to.

As discussed earlier, while a conventional new drug merits 5 years of exclusivity in the U.S.,[278] an orphan drug is granted 7 years of exclusivity[279] and a new indication is granted 3 years of exclusivity.[280] The period of protection for

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an%20Drug%20Act.pdf; *see also* Haffner *supra* note 248, at 445-7; *see also See* Linda C. Ulrich, *Efforts to develop orphan drugs: The FDA experience*, 12 PHARMACEUTICALS POLICY AND LAW 53, 54 (2010).

[277] *See* Labadie & Zhou, *supra* note 276, at 219 ("During the 1983–1989 period, 8 orphan drugs per year obtained FDA approval on average. From 1990 to 1999, this average had increased to 14 orphan drug approvals per year and in the 2000–2008 period, 15 orphan drugs per year obtained approval.").

[278] *See* 21 U.S.C. S. 355(j)(5)(F)(ii) (laying down that drugs based on NCEs, are entitled to an exclusivity period of 5 years); *see also* Dickinson, *supra* note 243.

[279] This exclusivity of 7 years is granted only to approved "orphan" drugs, defined under the Orphan Drug Act, 1983 as those products that treat rare diseases and conditions affecting less than 200,000 patients in the country. The Act is designed to combat the general unwillingness of pharmaceutical manufacturers to invest in the development of commercial drugs for the treatment of diseases which, although devastating to their victims, afflict too small a proportion of the population to make them commercially viable. Orphan Drug Act, Pub. L. No. 97-414, § 1(b)(4)-(5), 96 Stat. 2049, 2049 (1983) (Congress' findings); H. R. Rep. No. 840, 97th Cong., 1st Sess. 1, *reprinted in* 1982 U.S. Code Cong. & Admin. News 3577, 3577.

[280] This category includes any application for an existing drug (containing a previously approved active ingredient), for which a new use or indication has been discovered. Upon the generation of clinical trial data pointing to such new uses, new dosages or new indications, the said drug is entitled to 3 years of data exclusivity. Similarly for encouraging paediatric trials, an exclusivity of 6

biologics is even higher at 12 years.[281] The EU, on the other hand, provides a uniform period of protection of almost 11 years for most new drugs, as encapsulated in the commonly referenced 8+2+1 rule.[282] In contrast, a patent can be granted only when it is established that the claimed substance is patent eligible and patentable.[283] These pre-requisites have been the subject matter of countless legal disputes, resulting in a grant process that is often uncertain, expensive and time consuming.[284] While the drug regulatory process (and data exclusivity norms in particular) is also susceptible to interpretative disputes, it is relatively more determinate and less expensive to administer than the patent system. Secondly, and perhaps, more importantly, while a patent system rewards the mere prospect of an innovation, a data exclusivity regime rewards only instances of successful innovation (i.e. the final drug approval).[285] This disconnect between the incentive

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months is granted. Food and Drug Administration Modernization Act, 1997, § 111; paediatric exclusivity is unique in that it is not a stand-alone exclusivity protection, but attaches itself as an additional period to already existing periods of exclusivity that the drug is entitled to.

[281] *See* § 7002(k)(7) of the BPCI Act, 2009 in Title VII of the Patient Protection and Affordable Care Act, 2010.

[282] *See* European Commission, *supra* note 260.

[283] *See* Justine Pila, *Bound Futures: Patent Law and Modern Biotechnology*, 9(2) B.U.J. SCI & TECH. L. 326, 341-2 (defining 'patent eligibility' broadly). She notes:

> "Patent eligibility" broadly refers to the requirement that a subject matter for which a patent is sought be inherently suitable for patent protection, in the sense of falling within the scope of subject matter that patent law *prima facie* exists to protect. The term 'patentability', on the other hand, refers to those set of principles that inform the requirements that must be satisfied for a patent eligible subject matter (i.e., an invention) to be granted a valid patent. Principally they are the requirements of novelty, inventiveness (non-obviousness), utility (industrial applicability) and sufficient description.

[284] *See* discussion on relative indeterminacy of patent standards in Chapter II, *supra* text accompanying notes 191-212.

[285] *See* Heled, *supra* note 193, at 63-64 (noting that patent monopoly is granted only to a "worthy

of a patent system and the prospects of commercialisation has caused a scholar to advocate a separate "commercialisation" patent.[286] Further, unlike market protection through data exclusivity norms, upstream patents could potentially block the process of creating the drug itself i.e. downstream drug development.[287]

Owing to these various advantages inherent in a data exclusivity regime, commentators have favoured this regime over patents. A commentator tellingly notes:

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technology"). He argues:

> [s]tatutory exclusivities guarantee that only "worthy technologies" are granted monopolies. A constant concern in the context of technological advances is that monopoly grants may be squandered on "unworthy" technologies. For instance, it is not uncommon that inventions that lack any value to society are granted patents just because they happen to "satisfy" the requirements of patent law. As opposed to the patent examination process, which mostly utilizes standards not directly relevant to any particular technology, evaluation of new technologies by specialized agencies directly gauges the "social worth" of such technologies.

[286] *See* Sichelman, *supra* note 98, at 342 (criticising the present patent system and advocating a new 'commercialization' patent). He notes:

> [t]he patent system is substantially retarding the commercialization of valuable inventions. The result should not come as a surprise- the dominant framework undergirding the patent law, the "reward" theory, is premised on providing incentives for nascent inventions, not commercialised end products… I propose a new "commercialisation" patent, granted in exchange for the commitment to make and sell a substantially novel product**.**

[287] *See* Eisenberg, *supra* note 20, at 365-66 (comparing how patents and FDA administered exclusivities work in the context of drug development). She notes:

> First, the FDA provides product market exclusivity while the patent system provides invention exclusivity. Because many inventions are used in the course of product development, strengthening patent protection is a double-edged sword for innovating firms. While it fortifies the drug patents that provide product market exclusivity, it also fortifies the patents on the many proprietary inputs into drug development, thus adding to the costs as well as the revenues for drug-developing firms. FDA administered exclusivities, by contrast, enhance product revenues without increasing these costs.

> [S]tatutory exclusivities have numerous advantages over patents… patents are a cumbersome, inefficient and often ineffective way of "promot[ing] the Progress of Science and useful Arts." FDA granted statutory exclusivities, on the other hand, appear to be more comprehensive and easily enforceable, would significantly reduce costs involved in litigation, are less prone to abuse and would create legal certainty that is currently missing from the protection of technological innovation under patent law.[288]

Ben Roin and Brian Eller also support such a sentiment, although in the limited context of "unpatentable" drugs.[289] While these commentators are broadly correct in their assessment that data exclusivity is far more optimal than patents in fostering higher levels of R&D investment, they overlook a key deficiency in that data exclusivity regimes provide for uniform periods of protection. Secondly, most data exclusivity regimes cater primarily to investment costs in clinical trials (drug development). As this thesis demonstrates, the costs associated with drug

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[288] *See id.* at 364 (examining the merits and demerits of FDA-administered rules rather than through patent law in order to provide economic incentives for R&D) She notes:

> To the extent that legal regulation deliberately provides protection against competition in product markets as an economic incentive for R&D, one might ask whether it makes sense to provide such protection through FDA-administered rules rather than through patent law. Economic incentives for R&D are traditionally the province of the patent system, and arguably outside the core competence of the FDA in protecting public health. Nonetheless, there are advantages to using FDA regulation as a mechanism for providing product exclusivity.

*See also* Heled, *supra* note 193.

[289] *See* Roin, *supra* note 2, at 507 ("Moreover, since the FDA's regulatory requirements are themselves what drive much of the need for protection in the pharmaceutical industry, linking the reward of exclusivity to successfully completing clinical trials is a sensible approach to promoting innovation."); *see also* Brian B. Eller, *Promoting Innovation in the Pharmaceutical Industry by Expanding the FDA's Regulatory Powers to Grant Market Exclusivity* (UC Davis Legal Studies Research Paper, 2010), http://ssrn.com/abstract=1790566 (arguing on similar lines in favour of orphan drug exclusivity for those molecules that may have lost out in terms of patent protection, but require significant investments for its development).

discovery are not insignificant and ought to be compensated.[290] The problems in treating the current data exclusivity model as an optimal investment protection regime is discussed below.

### D. Problems with the Current Data Exclusivity Regime

Firstly, data exclusivity regimes are sub-optimal in that they set a "uniform" level of protection for all drugs, for the most part. As discussed earlier, the U.S. provides new "conventional" pharmaceutical drugs with 5 years of data exclusivity, while the EU provides a uniform 10 years for most conventional drugs. There is no persuasive evidence to suggest that any of the above time frames appropriately protect the significant investments made in drug development.[291] A recent study advocates that the length of protection for conventional drugs ought to be increased from 5 to 12 years.[292] It suggests that such an increase would increase the lifetime revenue of a drug by 5%, on average, lead to an additional 228 drug

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[290] *See supra* discussion in Chapter II: Patents, Investment Protection and Innovation, *supra* text accompanying notes 42-58.

[291] In 2007, the National Academies Committee on Science, Engineering, and Public Policy called for the United States to adopt the European data exclusivity period of 10 to 11 years. *See* NATIONAL ACADEMIES COMMITTEE ON SCIENCE ENGINEERING AND PUBLIC POLICY, *What Actions Should America Take in Economic and Technology Policy to Remain Prosperous in the 21st Century?*, *in* RISING ABOVE THE GATHERING STORM 182, 190 (2007), *available at* http://www.nap.edu/openbook.php?record_id=11463&page=190.

[292] *See* D.P. Goldman et al., *The Benefits from Giving Makers of Conventional 'Small Molecule' Drugs Longer Exclusivity over Clinical Trial Data*, 30(1) HEALTH AFFAIRS 84 (2011).

approvals over the next 50 years and an increase of 1.7 months in average life expectancy.[293]

The problem with such studies is that they attempt to draw out uniform conclusions for a wide range of drugs, without any enquiry into the individual costs per drug.[294] Consider the specific case of Makena, a drug taken to prevent pre-term births.[295] While attempting to defend its astronomical price, the pharmaceutical company in question, KV Pharmaceuticals stated that it spent more than U.S. $200 million to conduct trials and procure approval from the FDA. However, many believe that KV's price is excessive and would lead to significant overcompensation; it is estimated that the grant of a 7 year exclusivity period under the ODA, along with its current pricing of U.S. $1,500 per single shot would help it earn revenues of around U.S. $3billion, compensating it by a factor of about 15![296]

Roin believes that the current period of data exclusivity offered in the US is

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[293] *See id.* at 87.

[294] The U.S. discussion around biologics was a particularly heated one on this count, with several studies and papers advocating their version of what might be an ideal time frame for protection. Henry Grabowski, *Follow-on Biologics: Data Exclusivity and Balance between Innovation and Competition*, 7 NATURE REVIEWS DRUG DISCOVERY 479 (2008); *see also* John A. Vernon et al., *Exploration of Potential Economics of Follow-on Biologics and Implications for Data Exclusivity Periods for Biologics*, 16 B.U. J. SCI. & TECH. L. 55 (2010); *see* also Alex M. Brill, *Proper Duration of Data Exclusivity for Generic Biologics: A Critique* (Nov. 2008), *available at* http://www.tevadc.com/Brill_Exclusivity_in_Biogenerics.pdf.

[295] *See* discussion in Chapter IV: Investment Protection Regime, *infra* text accompanying notes 387-389.

[296] *After Makena: Could a Risk Corridors Approach Balance Incentives and Access?* (March 31, 2011), http://lawprofessors.typepad.com/healthlawprof_blog/2011/03/after-makena-could-a-risk-corridors-approach-balance-incentives-and-access.html

not sufficient and recommends that it be extended to anywhere between 10 to 14 years.[297] Roin argues that since this period effectively replicates patent style protection for the drug, it is optimal.[298] This is a questionable assumption; a far more defensible proposition would be to simply compensate the originator to the extent of actual expenses incurred in relation to a particular drug.

Secondly, apart from the above concerns relating to a uniform period of protection, existing data exclusivity regimes are deficient in that they aim to compensate only for the investments incurred during the clinical trial process, and not the significant expenses incurred during the upstream levels of drug discovery. As noted earlier, of the total U.S. $802 million stated to be the average cost associated with drug discovery and development, the costs associated with the drug discovery phase amount to U.S. $335 million, which is not an insignificant amount.[299]

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[297] *See* Roin, *supra* note 2. ("[b]y lengthening that period to somewhere between ten and fourteen years, Congress would at least provide a rough substitute for patent protection, and thus, eliminate the distortions arising from the novelty and non-obviousness requirements.")

[298] *See* Eller, *supra* note 289 (assuming that a 7 year orphan drug exclusivity term protection would incentivise drug development in so far as unpatentable drug molecules are concerned). He argues:

> [G]ranting the FDA the power to grant market exclusivity for seven years to any new drug or therapy that the FDA approves, as long as that drug or therapy has not been sold nor is being sold in the United States, has not been covered nor is currently covered by any US patent or US patent application, and has been covered in a publication that has been in existence for more than two years… The term of seven years is a term borrowed from the Orphan Drug Act and is intended to balance the needs of the general public for competitive drug pricing through generic competition, while giving drug companies sufficient market exclusivity to encourage innovation.

[299] It must be noted that these costs have been revised significantly and the latest estimates suggest U.S. $1.3 billion. However, the U.S. $802 and U.S. $335 million figure broadly indicate the proportion of costs between drug discovery and development.DiMasi et al., *supra* note 6, at 165.

Thirdly, standard data exclusivity models are linked with the regulatory process in significant ways, constraining their ability to operate as "innovation" fostering instruments.[300] Save orphan drugs, which are granted a comprehensive market exclusivity, the regular data exclusivity regime does not foreclose competitors from conducting their own tests, generating data and procuring drug approvals, such that they can enter the market without having to wait for the expiry of the exclusivity period in favour of the originator.

Lastly, it bears noting that although there are hardly any instances of generic entrants conducting their own clinical trial testing to avoid the originator exclusivity periods, the possibility does exist.[301] Where such possibility translates to action, the result is problematic from an ethical perspective, as human beings

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[300] *See* Katz, *supra* note 273; *see also* Eisenberg, *supra* note 20, at 359-60 (arguing that the innovation inducing rationale of data exclusivity regimes ought to be recognised more explicitly). She notes:

> [l]egislative initiatives have cast the FDA in the role of administering pharmaceutical pseudo-patents, unabashedly directing the FDA to use its market gatekeeper role to provide firms with market exclusivity in exchange for investing in certain kinds of pharmaceutical R&D. An early example of this is the Orphan Drug Act of 1983, which directs the agency to grant seven years of market exclusivity for products to treat rare diseases and conditions affecting fewer than 200,000 patients in the United States. In effect, these provisions amount to FDA-administered proprietary rights in regulatory data, awarded to encourage particular kinds of innovation in drug development rather than to protect consumers from unsafe or ineffective drugs.

[301] It bears noting that in the context of biologics, many firms opt to conduct their own trials for follow-on versions. Robert J. Shapiro et al., *The Potential American Market for Generic Biological Treatments and the Associated Cost Savings* (Feb. 2008), *available at* http://www.insmed.com/pdf/Biogeneric_Savings.pdf.

have to be subjected to another round of testing with the same drug.[302] The Helsinki Declaration effectively prohibits such unethical testing.[303] It specifies that, "[p]hysicians must immediately stop a study when the risks are found to outweigh the benefits or where there is conclusive proof of positive and benefit results."[304]

A data exclusivity regime encourages duplicative testing of an approved drug on human subjects, despite the fact that there already exists valid regulatory proof of its positive and beneficial results.[305] The spirit of the Helsinki Declaration would suggest that additional testing on human beings ought to be avoided and that follow on manufacturers must be permitted to rely on originator data.[306] To this extent, the models recommended in this thesis are in conformity with the spirit of the Helsinki Declaration.

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[302] *See* Junod *supra* note 38, at 486; *see also* R. Rajkumar, *The Central American Free Trade Agreement: An End Run Around The Doha Declaration on TRIPS and Public Health,* 15 ALB. L. J. SCI. & TECH. 433, 450 (2005).

[303] *See* Michael D. E. Goodyear & Trudo Lemmens, *The Declaration of Helsinki- Mosaic tablet, dynamic document, or dinosaur?*, 335 BRIT. MED. J. 624 (2007).

[304] The Declaration of Helsinki was first adopted by the World Medical Association in 1964 and is viewed as a successor to the Nuremberg Code dealing primarily with the ethical principles involved in human experimentation. Article 20, World Medical Association (WMA) Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects (2008), *available at* http://www.wma.net/en/30publications/10policies/b3/17c.pdf.

[305] *See* Letter from Bernard Sanders, US Senator for Margaret Hamburg, Commissioner of FDA (Nov. 2, 2010), *available at* http://www.fdalawblog.net/files/bpci-act---sanders-ltr-11-2010.pdf.

[306] *See* Jacqueline Fox, *Reinvigorating the Concept of Benefit: The Failure of Drug Sponsored Research on Human Subjects*, 38 SETON HALL L. REV. 605, 646 (2008).

For all the above reasons, I argue that a comprehensive investment protection regime, as recommended in this thesis is a far more optimal instrument than the current data exclusivity framework.

## CH. IV: INVESTMENT PROTECTION REGIME

The central argument of my thesis is that when compared with patents and data exclusivity, a comprehensive investment protection regime is a better instrument to foster accelerated levels of investment in drug discovery and development. Listed below are the core attributes of the proposed regime:

i) Requiring the drug originator to submit all costs relating to drug discovery and development;

ii) Granting market protection to drug originators till such time as they recover their total costs along with a reasonable rate of return on investment, dependant on the health value of the drug.

I consider two alternative models of investment protection in this thesis:

i) A standard exclusivity model, where the drug originator is granted a term of exclusivity during which no competitor can enter the market;

ii) A compulsory licensing or compensatory liability model, where competitors can enter the market after paying a reasonable compensation to the originator.

Owing to the propensity of market exclusivity models to engender excessive prices, I advocate a compulsory licensing/compensatory liability model and propose a novel methodology of computing compensation in this regard.

I begin the discussion by considering (in the Section below) the key challenges in determining the total costs of drug discovery and development, and an appropriate rate of return on investment for the inventor.

### A. Computing the Costs of Drug Discovery and Development

Despite pharmaceutical patents being one of the most debated issues today,[307] the extent of costs incurred in drug discovery and development remains highly contested. As noted earlier, the most widely circulated figure of U.S. $802 million (and updated more recently to U.S. $1.3 billion) has been challenged by several critics.[308]

Fortunately, the investment protection regime advocated by this thesis saves us the trouble of validating these figures. Rather, it simply asks for the costs per individual drug. This is a relatively easier endeavour than attempting to identify average costs across a wide entire spectrum of drugs, as DiMasi and other

[307] *See* Joseph Stiglitz & Arjun Jayadev, *Medicine for tomorrow: Some alternative proposals to promote socially beneficial research and development in pharmaceuticals*, 7 J. GENERIC MEDICINES 217 (2010).

[308] *See supra* text accompanying notes 47-50.

scholars have previously done. The regime proposed in this thesis requires each company to disclose its total costs upfront. Such costs would ordinarily include:

i) all "discovery" and "development" expenses incurred in relation to a drug that is approved by a drug regulator;

ii) all fixed costs for establishing the relevant manufacturing facility, provided the facility has been created specifically for the drug in question; and

iii) the costs of all tried and tested targets and leads in relation to a particular disease.[309]

The terms "discovery" and "development" as used in the first category have already been defined in Chapter I of the thesis. While most commentators focus on the downstream drug development phase (the clinical trial phase), as one characterised by intensive investments and therefore worthy of protection,[310] it bears noting that the upstream drug discovery phase also entails significant expenditure. DiMasi et al. estimate that when compared to the total costs associated with drug discovery and development (U.S. $802 million), the costs of

[309] *Compare* DiMasi et al., *supra* note 6, at 152-3 (stating the estimates made that included the cost of failures), *with* Avance, *The U.S. $1 Billion Drug: A Fairytale,* News in Avance, (Dec. 2007), *available at* http://www.avance.ch/newsletter/docs/avance_on_dimasi.pdf (criticising and questioning the inclusion of failures in these figures).

[310] *See* Faiz Kermani & Pietro Banacossa, *Patent Issues and Future Trends in Drug Development*, 9 J. COMM. BIOTECH. 332 (2003); *see also* Sichelman, *supra* note 98, at 387.

drug discovery (U.S. $335 million) are not significantly lower than that of drug development (U.S. $467 million).[311]

The thesis, therefore, proposes an inclusion of all costs incurred during both the discovery and development stages. The question then is: how far back into the "discovery" process ought one to traverse into, in order to compute such costs? Chapter I described the various stages associated with drug innovation processes and defined "drug discovery" as the stage commencing with the search for a disease target. This is a more realistic cut-off than pre-clinical testing or an IND filing. While such stages may make for a relatively easier cut-off they ignore important steps which precede them.

In order to contextualise the discussion, consider the evolution of Glivec,[312] a path-breaking anti-cancer drug that is now the subject of a highly contentious patent litigation in India.[313] Touted as a "wonder drug,"[314] Glivec treats chronic myeloid leukemia (hereinafter "CML"), a cancer of myeloid blood cells characterised by a proliferation of granulocytes in the blood and bone marrow.

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[311] *See* DiMasi et al., *supra* note 6, at 166.

[312] *See* Novartis Pharmaceuticals Corporation, *About Gleevec*, *available at* http://www.gleevec.com/patient/gleevec-prescription-medication-information.jsp (last visited Sept. 30, 2011**)** (stating that 'Glivec' was marketed as 'Gleevec' in the US for the use of chronic myloid leukemia).

[313] *See* Shamnad Basheer & T. Prashant Reddy, *The "Efficacy" of Indian Patent Law: Ironing Out the Creases under Section 3(d)*, 5(2) SCRIPT-ED 234, 235-8 (2008).

[314] *See* Elisabeth Buchdunger & Juerg Zimmercan, *The Story of Gleevec*, *available at* http://www.innovation.org/index.cfm/StoriesofInnovation/InnovatorStories/The_Story_of_Gleevec (last visited Sept. 30, 2011).

More than 90% of people with CML have an acquired chromosomal abnormality, called the Philadelphia chromosome, caused by reciprocal translocations between chromosomes 9 and 22. These translocations result in a BCR-ABL fusion gene that codes an active tyrosine kinase protein, which in turn leads to uncontrolled cell proliferation.

A newly discovered molecule, Imatinib, was found to inhibit Tyrosine Kinase and thereby slow down the progression of CML. The various steps in the discovery and development of Glivec can be broken down as below:

1. Discovery of the Philadelphia Chromosome (a genetic mutation found in patients with CML): 1960
2. Discovery that the genetic abnormality results in a cancer-inducing kinase enzyme: 1980s (note that this enzyme is effectively the "target" that any potential drug must inhibit).
3. More than 400 compounds are screened to assess their potential in inhibiting the "target" enzyme: late 1980s
4. Scientists identify STI471 (Imatinib) as the most promising "lead" that could inhibit the enzyme, without affecting other cells: 1992[315]

[315] This piece describes how in early 1990, Dr. Elisabeth Buchdunger and Dr. Juerg Zimmerman, employees of Novartis, accepted a challenge from the leaders of the tyrosine kinase inhibition team - Nick Lydon and Alex Matter. They had to refine the lead compound that blocks the enzyme that triggers CML without harming other members of the same family, called kinases that are needed for the body to function. Two years and some 400 molecules later, the researchers and their colleagues came up with the molecule that finally became Glivec. *Id*.

5. Novartis files a patent covering Imatinib (free base) and all pharmaceutically acceptable salts: 1993[316]

6. Novartis files a patent covering the beta crystalline version of Imatinib Mesylate, the active ingredient underlying the drug, Glivec: 1997[317]

7. Glivec is granted FDA approval: 2001[318]

Under the model proposed in this thesis, all costs incurred after Step 2 (identification of the target i.e. cancer-inducing kinase enzyme) are included in the total costs of drug discovery and development, and is eligible for compensation.[319]

**1. Cost of Failure**

Given that the proposed regime covers all drug discovery costs, it effectively compensates for failure as well. Failure in such a context refers to those leads that are tested for a particular disease, but do not make it past the regulatory filter. Typically, for every lead that makes it past the regulatory filter, there are several others that had been tested for the same target, but failed to demonstrate sufficient safety and efficacy as to merit regulatory drug approval. Given that such failures are often routine in the drug discovery and development process, this thesis advocates

[316] *See* U.S. Patent No. 5521184 (April 1993).

[317] *See* U.S. Patent No. 6894051 (January 2000) (The patent was first filed in Switzerland in July 1997 and then subsequently in the US in 2000, claiming priority from the Swiss filing.)

[318] *See* Novartis Pharmaceuticals Corporation, *supra* note 312.

[319] *See* Basheer & Reddy, *supra* note 313.

for the inclusion of costs associated with such failures as well.[320]

Further, it might also be the case that none of the leads tested for a certain target gain regulatory approval. Therefore, it is important to permit a drug originator to recover its costs, associated with all targets that are pursued within the framework of a single disease. This would encourage drug originators to take more risks, knowing that even if the target chosen did not end up a winner, the costs relating to exploring that particular target could still be covered.

It bears reiteration that regulatory clearance is becoming increasingly difficult, with only about 19% of the drugs entering the clinical stage being finally approved by the U.S. FDA.[321] The Pharmaceutical Research and Manufacturers of America (PhRMA) and the European Federation of Pharmaceutical Industries and Associations (EFPIA) exemplify the high rate of failure by noting that, for every 5,000 drugs tested, only 5 make it to clinical trials on an average, and of those 5, only 1 is ultimately approved for patient-use.[322] Given this high regulatory risk, it is only fair that the cost of failed "leads" and targets be included, as this is a

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[320] *See* Meena K. Sakharkar et al., *Quantitative analysis on the characteristics of targets with FDA approved drugs*, 4 INT. J. BIO. SCI. 15 (2008), *available at* http://www.biolsci.org/v04p0015.htm#B19 (last visited Sept. 30, 2011) (noting that experience from the biopharmaceutical industry indicates that currently only 5% of newly explored targets eventually lead to FDA-approved products).

[321] *See* DiMasi et al., *supra* note 6.

[322] *See* Fellmeth, *supra* note 42, at 495 *see also* Maggie Fox, *US takes step to Government Drug Development Center*, (December 7), 2010, *available at* http://www.reuters.com/article/2010/12/07/us-usa-institute-idUSTRE6B66ZG20101207 (last visited Sept. 30, 2011).

"legitimate" cost incurred even by the best of innovators.[323] However, all costs have to necessarily relate to investigations pertaining to a single disease.

### 2. Excluded Costs

The above discussion focussed on the kind of costs that ought to be recompensed under an investment protection regime. It is equally important to discuss the kind of costs that ought to be excluded in order to avoid over-compensating the investor. Firstly, the costs that have already been claimed in relation to an originator drug cannot be reclaimed for a second derivative drug.[324] By way of example, any R&D expenses incurred in relation to the development of Prilosec ought to be excluded from the costs associated with its derivative, Nexium. Both are proton pump inhibitors developed by Astra Zeneca to cure acidity.[325] Secondly, as discussed earlier, any public funds made available to the drug originator ought to be deducted from the overall costs of drug discovery and development, while assessing the extent of protection owed to such drugs under the proposed regime.

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[323] *See* Thomas A. Abbott & John A. Vernon, *The Cost of US Pharmaceutical Price Reductions: A Financial Simulation Model of R&D Decisions*, 12-13 (National Bureau of Economic Research (NBER), Working Paper 11114, 2005), *available at* http://www.nber.org/papers/w11114.pdf; *see also* Fellmeth, *supra* note 42 (recommending something similar).

[324] This is to prevent any double counting of costs which, as we have already discussed been cautioned against by several critics of the industry endorsed drug development figures. Light, *supra* note 55, at 326.

[325] *See infra* text accompanying notes 454-457.

### B. Submission of Information Relating to Profits

Apart from a mandatory submission of costs, pharmaceutical firms that wish to protect their investments under the proposed regime are required to submit estimates of yearly revenues and profits. These submissions would enable a computation of profits year after year until such time as drug originators recover their costs and an appropriate rate of return on investment depending on the health impact of the drug.

In order that competing firms might track the effective period of exclusivity resulting from the operation of this model, and prepare for launching generic versions, the following mechanism is proposed:

Upon the total profits earned by a drug originator nearing the overall costs incurred in relation to that drug, the originator must begin submitting a monthly estimate of its profits. Any follow-on manufacturer can file an application for regulatory approval of their generic version even prior to the expiry of the effective exclusivity period, and such approval shall be granted, if the pre-requisite regulatory standards are met. However, the competitor cannot launch its drug till such time as the exclusivity expires.

Although ascertaining costs and the profits of pharmaceutical firms in an objectively determinate manner is a difficult task and may be subject to inflation

and manipulation in the initial years, it can be expected that after the regime has operated for some years, it will engender more accurate reporting of costs and revenue figures.[326] In particular, government administrators of such a regime will, over time, become more adept at scrutinising the veracity of submitted figures.

### C. The Investment Protection Regime in Operation

The operation of the investment protection regime is best exemplified through the following illustration. Assume that "*X*", a pharmaceutical firm, obtains regulatory approval for drug "*A*" in the US. The total cost of discovery and development of the drug up to the time of approval is U.S. $800. Under the model proposed in this thesis, *X* has to be granted a legal monopoly (exclusivity in the market) until such time as *X* recovers this amount, as also the normal bank rate of interest and a rate of return on investment based on the health impact of the drug. Let us assume that the highest available bank rate of interest (amongst various banks and financial institutions) is 10%. Let us also assume that the health impact of the drug merits a rate of return on investment of 15%. The total rate of return on investment is, therefore, 25%.

The model operates in a manner such that *X* is granted legally sanctioned market exclusivity until *X*'s investments are recovered, along with the requisite rate of

[326] Costs of R&D are routinely submitted in countries that offer tax incentives for R&D projects. Lessons from this process, such as the form in which such expenses are submitted and the ways in which over inflation is guarded against could be drawn from in this context as well.

return on investment. In this case, it would be U.S. $1,000 (U.S. $800 + 25% rate of return on investment). If the bank rate varies widely during the exclusivity period, the last year of payment (the year in which the originator comes to be fully and finally compensated) could be adjusted to account for this variation.

## D. Measuring Health Impact

The appropriate rate of return on investment to a pharmaceutical investor would largely depend upon the health impact of a drug. Several measures exist to determine such impact, and I discuss two of the most prominent metrics in this regard:

i) Quality Adjusted Life Years (QALY)

ii) Disability Adjusted Life Years (DALY)

Each of these is explained below:

### 1. QALY

Quality Adjusted Life Years (hereinafter "QALY") is an economic tool for assessing the relative worth of health care interventions while making funding decisions.[327]

[327] *See* Amanda Brower, *Is it Time To Take a Harder Look at the QALY?*, 5(3) BIOTECHNOLOGY HEALTHCARE 47, 48 (2008); *see also* Ceri Phillips, *What is a QALY?* (2009), HAYWARD MEDICAL COMMUNICATIONS, http://www.medicine.ox.ac.uk/bandolier/painres/download/whatis/QALY.pdf.

The use of this metric was widely popularised by the National Institute for Health and Clinical Excellence (hereinafter "NICE"), a U.K. based authority entrusted with the responsibility of choosing drugs that are therapeutically valuable and cost effective to warrant National Health Services (hereinafter "NHS")[328] procurement.[329]

QALY is defined as the "measure of a person's length of life weighted by a valuation of their health-related quality of life."[330] Generally, a QALY score is the product of the number of years in a particular state of health and the utility assigned to that state. The different states of an individual's health are categorised on a scale ranging from 0-1.[331] While "0" represents death, "1" is the best-possible

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[328]*See* NHS, *About the NHS,* http://www.nhs.uk/NHSEngland/thenhs/about/Pages/overview.aspx. (last visited Sept. 30, 2011) (stating that the NHS is a publicly funded health service providing free medical care to residents in the United Kingdom); *see also* NICE, *NICE and the NHS*, http://www.nice.org.uk/aboutnice/whatwedo/niceandthenhs/nice_and_the_nhs.jsp (last visited Sept. 30, 2011) (stating that NICE provides the NHS with guidance on public health, clinical guidelines, technology appraisals and interventional procedures amongst others).

[329] *See* Canadian Agency for Drugs and Technologies in Health, *The Economic Value of Innovative Health Technologies* (2011), *available at* http://www.cadth.ca/media/pdf/H0495_Protocol_e.pdf (explaining that QALY is also used in Canada by the Canadian Agency for Drugs and Technologies in Health (CADTH), a non-profit agency funded by the Canadian federal and provincial governments to provide information about effectiveness of drugs and other health technologies to Canadian health care decision makers); *see also* European Commission, *From assessing Innovative Value of Pharmaceuticals to Pricing and Reimbursement Decisions*, *available at* http://ec.europa.eu/pharmaforum/docs/pricing_assessing_en.pdf. (last visited Sept. 30, 2011) (noting that in France, however, the Haute Autorité de Santé (HAS) (French National Authority for Health) evaluates the added value of new drugs through a body of experts who vote on a scale of 1 (major improvement) to 5 (no improvement)); *see also* Bruno Falissard et al., *Relative Effectiveness Assessment of Listed Drugs (REAL): A new method for an early comparison of the effectiveness of approved health technologies*, 26(1) INT'L. J. TECH. ASSESS. HEALTH CARE 124 (2010).

[330]*See* NICE, *Guide to Methods of Technology Appraisal*, (NICE, 2008), http://www.nice.org.uk/media/B52/A7/TAMethodsGuideUpdatedJune2008.pdf.

[331]*See* NICE, *Measuring Effectiveness and cost effectiveness: the QALY*, http://www.nice.org.uk/newsroom/features/measuringeffectivenessandcosteffectivenesstheqaly.jsp (last visited Sept. 30, 2011).

state of health. Different values prevail under different classification systems. Illustratively, the EuroQOL-5 used by NICE assigns values for around 243 health states, based on five parameters which include mobility, pain or discomfort, self-care, anxiety or depression and usual activities.[332] These scores are based on random population surveys comprising of approximately 3,000 people in the U.K.[333] Contrast this with the Human Utilities Index (hereinafter "HUI"), which takes only 7 or 8 parameters into account.[334]

QALY facilitates a cost-benefit approach to determining the relative advantages of funding a new health intervention *vis-à-vis* an existing treatment, or against no treatment at all.[335] To substantiate, assume that for a patient about to die, a new drug provides a life expectancy of 5 years at a quality of life valued at 0.7, whereas the standard treatment provides a life expectancy of 1 year with a quality of life at 0.3. The QALY value of the new drug is 3.5 (0.7 x 5) and the gain from the new drug, as compared to the standard treatment is 3.2 (3.5 - 0.3). Assuming the new drug costs £ 5,000 per year and the standard drug costs £ 1,000, the difference

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[332] *See* Marilyn Dix Smith et al., *Moving the QALY Forward: Rationale for Change*, 12 (1) VALUE IN HEALTH S1, S2 (2009).

[333] *See* Phillips, *supra* note 327.

[334] *See* Milton Weinstein et al., *QALYs: The Basics*, 12(1) VALUE IN HEALTH S5, S7 (2009) (noting that the Health Utilities Index Mark 2 scale uses seven parameters whereas the Mark 3 scale uses eight); *see also* George W. Torrence et al., *Multiattribute Utility Function for a Comprehensive Health Status Classification System*, 34(7) MED. CARE 702 (1996) (noting that the seven parameters in HUI:2 are sensation, mobility, emotion, cognition, self-care, pain and fertility); *see also* Frank Mo et al., *Using Health Utility Index (HUI) for Measuring the Impact on Health-Related Quality of Life (HRQL) among Individuals with Chronic Diseases*, 4 SCIENCE. WORLD J. 746 (2004) (noting that the eight parameters in HUI:3 are vision, hearing, speech, mobility, dexterity, cognition, emotion and pain/discomfort).

[335] *See* R. Kirkdale et al., *The Cost of a QALY*, 103(9) QJM 715 (2010).

is £ 24,000 and the cost per QALY works out to £ 7500 per QALY (i.e. 24,000/3.2).[336] NICE has adopted a range of £ 20,000 to £ 30,000 as the standard cost per QALY, which is considered cost-effective.[337] The QALY scores of new drugs as determined by NICE are then relied upon by the NHS for the purpose of assessing whether or not such a drug ought to be subsidised by it.[338]

While the QALY framework is routinely deployed to compute the relative cost-effectiveness of a drug, the investment regime proposed in this paper requires a stand-alone "health" value for the drug being assessed. The following example is illustrative of how the QALY framework might work in such a context:

1. Let us assume that the average life expectancy of a person, "*X*" residing in country "*A*" is 70 years.

2. *X* contracts an illness at the age of 50 years. Owing to this illness, her life span is reduced to 60 years i.e. he has only 10 more years to live. Let us assume that *X*'s disease is assigned a health state of "0.5" (a perfect QALY health score is "1")

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[336] *See id.*

[337] *See* Smith et al., *supra* note 332. (arguing that the threshold set by NICE is an arbitrary figure, having no basis in either theory or evidence); *see* John Appleby et al., Editorial, *NICE's Cost Effectiveness threshold*, 335 BRIT. MED. J. 358 (2007), *available at* http://www.bmj.com/content/335/7616 /358.full (last visited Sept. 30, 2011).

[338] *See* NICE, *supra* note 328; *see also* The National Institute for Clinical Excellence (Establishment and Constitution) Order, 1999 (Eng.).

3. The total QALY score for *X* in the present diseased condition is "5" (10 times 0.5, where 10 represents the number of years left and 0.5 represents the expected health state for all those years).

4. Let us assume that a new drug (*D*) will not rid *X* of the ailment, but will mitigate the impact of the disease, resulting in a health state whose value is 0.8. It will also enable him to live for 2 extra years i.e. 12 years. *X*'s QALY score after the drug intervention is 9.6 (12 times 0.8)

5. Since *X*'s QALY score has increased from 5 to 9.6, the benefit of drug D is 4.6.

6. Any subsequent drug for the same disease has to be judged against the existing drug. Therefore, a better drug for this disease (*D1*) which helps X live for 15 years, i.e. 3 extra years at a health state of 0.9, will have a QALY score of 13.5 (15 times 0.9), but its relative benefit would only be 3.9 (i.e. 13.5 less 9.6).[339]

Although a QALY score helps one assess the health impact of a drug, it is far from perfect. While there are several critiques of the QALY framework, I consider two of the most prominent ones. Firstly, QALY values have been questioned on the ground that they are judged *ex ante* by the general public, who do not have any direct

[339] The result, therefore, is analogous to the novelty, non-obviousness etc. criteria used to judge an invention's departure from the prior art in case of a patent. In our case, however, the difference is quantified and rewarded proportionately.

experience with the relevant diseased state.[340] The computation framework must, therefore, improve such that it measures "experienced" utility by those that are or have been impacted by the diseased state. Secondly, QALYs are often criticised for having an implicit ageist bias, in that there is a preference for saving the lives of younger people who are economically more productive to that of saving lives of the elderly.[341] The QALY metric must, therefore, be re-modelled to remove this ageist bias.

**2. DALY**

Disability Adjusted Life Years (hereinafter "DALY") is another metric that is used to measure the impact of a disease and the value of an intervention to cure that disease. The DALY framework was developed by the World Health Organisation (hereinafter "WHO") experts to measure the loss caused by particular diseases, particularly premature deaths and disabilities.[342] Its key advantage lies in the fact that it has been specifically adapted to capture disease incidence and prevalence, and is therefore, useful for measuring health values for large patient populations and developing country diseases.

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[340] *See* Erik Nord, *QALYs: Some Challenges*, 12(1) VALUE IN HEALTH S10 (2009).

[341] *See* John Harris, *It's not NICE to discriminate*, 31 J. MED. ETHICS 373 (2005). *See* also John Harris, *Qualifying the Value of Life,* 13(3) J. MED. ETHICS 117, 119 (1987).

[342] *See* C.J.L. Murray & A. Acharya, *Understanding DALYs*, J. HEALTH ECON. 703 (1997).

The "years of life lost" (hereinafter "YLL") is a measure of the number of years of life lost due to premature mortality brought about by the disease. This is calculated using the standard life expectancy at the age of death. The standard life expectancy at birth is set at 82.5 years for women and 80 years for men, and YLL is the difference between the standard life expectancy and the number of years lived (including the years lived with the disability or disease).[343]

The "years lived in disability" (hereinafter "YLD") on the other hand, is measured as a product of the average number of years lived in disability and the disability weight assigned for that particular health state.[344] Disability weights are calculated by taking into account the different health states of individuals with a range of 0-1, where "1" represents death and "0" represents perfect health.[345] These weights were designed by health experts of different regions[346] and a deliberative system following the "person trade-off" method was adopted, whereby participants were asked to trade-off life extension of healthy individuals and life extension of individuals in a given diseased state.[347] Under this method, the

[343] *See id*. at 711.

[344] *See* J.A. Fox-Rushby & K. Hanson, *Calculating and Presenting Disability Adjusted Life Years in Cost-effectiveness Analysis*, 16(3) HEALTH POL. & PLANN. 326, 328 (2001).

[345] *See* Trude Arnesen & Erik Nord, *The Value of DALY: Problems with Ethics and Validity of Disability Adjusted Life Years*, 319 BRIT. MED. J. 1423 (1999).

[346] *See* Murray & Acharya, *supra* note 342, at 713.

[347] The person trade-off method involves questions such as whether the decision maker would prefer 1 year of life for 1000 perfectly healthy individuals or 'n' number of disabled individuals. The second question involved evaluations of specific chronic conditions. These questions were answered independently by experts and then debated upon. Based on this, 22 conditions were categorized into

disability weight for blindness due to glaucoma yielded a score of 0.6, impotence yielded 0.06 and infertility yielded 0.18, respectively.[348] For cancer, the disability weight was 0.75 in the metastasis stage and 0.81 in the terminal stage.[349]

The term "disability" in this context simply means the loss of health, where health connotes functioning capacity in a set of health-related domains such as mobility, cognition, hearing and vision.[350] To this extent, the disability weights in DALY are exactly the inverse of QALY weights i.e. lower DALYs signify better health, whereas lower QALYs imply poorer health. The advantage with DALYs, however, is that it not only measures the cost-effectiveness of a particular health intervention, but also the global burden of disease. The WHO uses the DALY metric to make assessments on the incidence, prevalence, duration and severity of a wide range of conditions.[351] It also deploys discounting and age-weighting to give lesser weight to years lived at very young and at older ages.[352] Consequently, a death in infancy

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7 classes which were assigned disability weights. For a discussion on this, see Arnesen & Nord, *supra* note 345.

[348] *See* WHO, *Global Burden of Disease 2004 Update: Disability Weights for Diseases and Conditions*, *available at* http://www.who.int/healthinfo/global_burden_disease/GBD2004_DisabilityWeights.pdf.

[349] *See id.*

[350] *See id.*; *see also* Theresia Degener, *Definition of Disability (EC Action Program to Combat Discrimination Study, 2001-06)*, *available at* http://www.nuigalway.ie/law/Disability_summer_school/Docs/2006/Marc%20De%20Vos%20Teaching%20Materails%202%20%20Definition%20of%20Disability.rtf (noting that the legal definition of 'disability' is otherwise fraught with difficulties and obstacles).

[351] *See* WHO, *Global Burden of Disease: 2004 Update,* 40 , *available at* http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf.

[352] *See* WHO, *Disability Weights, Discounting and Age Weighting of DALYs*, http://www.who.int/healthinfo/global_burden_disease/daly_disability_weight/en/index.html (last

corresponds to 33 DALYs, whereas deaths at ages 5-20 years equate to approximately 36 DALYs.[353] Using the above framework, the WHO found that:

i) Respiratory infections caused the highest global burden of disease, with 94.5 million DALYs or 6.2% of the total disease burden.[354]

ii) HIV/AIDS ranked amongst the top 5, securing 3.8% of the total DALYs.[355]

iii) Tuberculosis and Malaria were 11th and 12th on the list respectively, with each securing approximately 2.2% of the total DALYs.[356]

Though originally developed for calculating the global burden of diseases, DALYs have also been used for the measurement of cost-effectiveness of specific health interventions. In such cases, in addition to age-weights and discount rates, it is also necessary to know the disability weights associated with different states of disability and the changed states brought about by an existing treatment and the proposed new treatment.[357] Illustratively, a DALY metric was used for assessing the cost-effectiveness of Sulfadoxine-pyrimethamine (SP), a first line treatment for

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visited Sept. 30, 2011); *see also* Franco Sassi, *How to do (or not to do)…Calculating QALYs, comparing QALY and DALY calculations*, 21(5) HEALTH POL. & PLANN. 402, 404 (2006).

[353] *See* WHO, *supra* note 351, at 3.

[354] *See id.* at 43.

[355] *See id*.

[356] *See id.*

[357] *See id* at 45.

averting malaria amongst infants in two small rural areas in Africa, Ifkara in Tanzania and Manhica in Mozambique.[358] The number of DALYs averted were estimated at 118.9 per thousand infants for Ifakara, and 46.7 for Manhica.

The DALYs averted were calculated by combining the burden of disease averted due to decreased malaria morbidity (as a function of malaria incidence, disease duration and impact on quality of life) and malaria mortality (as a function of malaria incidence, case-fatality rate and average life expectancy at age 1 year). The cost-effectiveness comparison was made with respect to a "do-nothing" scenario and it was found that the cost per DALY averted was under U.S. $12 at both the sites surveyed.[359] On this basis, this treatment was held to be cost-effective in both these regions.[360]

DALYs and QALYs are technically similar in that they both express health in terms of time (life years) and attribute differential weights to diseases, depending on their impact on patients. In the terminology of Gold et al., both measures are

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[358] *See* Guy Hutton et al, *Cost-effectiveness of malaria intermittent preventive treatment in infants (IPTi) in Mozambique and United Republic of Tanzania*, 87 BULL. WORLD HEALTH ORGAN 123 (2009), http://www.who.int/bulletin/volumes/87/2/08-051961/en/index.html.

[359] *See id.*

[360] The threshold for cost-effectiveness was calculated on the basis of the gross national product (GNP) per person in Africa, and the intervention was described as 'attractive' if it fell below U.S.$150 per DALY and 'highly cost-effective' if it fell below U.S. $25. C.A. Goodman et al., *Cost-effectiveness of Malaria Control in Sub-Saharan Africa*, 354 (9176) LANCET 378, 379 (1999).

Health Adjusted Life Years (hereinafter "HALYs").[361] Although QALYs and DALYs may yield different outcomes, such differences are largely attributable to the use of different disease weights and the use or otherwise of weighting and discounting in appropriate cases.[362]

As with QALY, the DALY framework has also been criticised. Firstly, Rushby and Hanson point out that it has not yet been operationalised as a tool for collecting data alongside experimental or quasi-experimental trials of health interventions.[363] As a result, the values obtained for health states post treatment/intervention may lack "experiential" value. Secondly, DALYs have been criticised on ethical grounds due to the trade-off between the lives of the healthy and the disabled, where the former are preferred to the latter.[364] Further, the manner of calculation of the disability weights includes two different person trade-off questions. With each question given an independent weight, the consistency between them may be deliberated and forced.[365] Thirdly, the computation of DALYs across populations is likely to lead to a serious disincentive for companies to invest in "orphan drugs," or drugs for the treatment of rare diseases, an aspect that has been critiqued by

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[361] *See* Marthe R. Gold et al., *HALYs and QALYs and DALYs, Oh My: Similarities and Differences in Summary Measures of Population Health*, 23 ANN.. REV. PUBLIC HEALTH 115 (2002).

[362] A comparison of the QALY and DALY metrics for two conditions, one potentially fatal (bipolar depression) and the other non-fatal (tuberculosis) showed that the variation was largely attributed to the age of onset of the disease, thereby originating from the shape of the age-weighing function. Sassi, *supra* note 352, at 407.

[363] *See* Rushby & Hanson, *supra* note 344, at 329.

[364] *See id*.

[365] *See* Arnesen & Nord, *supra* note 345.

several authors.[366] The DALY framework must, therefore, be amended to give equitable consideration to orphan diseases.

The use of standardised life expectancies in measuring the global burden of disease is disputed, since these figures are considerably higher than the life expectancy rates in most developing countries.[367] This problem can be avoided by using a localised expectancy rate, as recommended by Murray & Lopez.[368]

Notwithstanding these various criticisms, I argue that these health assessment tools are advantageous, in that they strengthen the case for directing R&D resources towards more impactful drugs.[369] In other words, the adoption of a QALY or DALY score, albeit an imperfect one, is likely to yield a better outcome than the present patent reward structure which incentivises a variant of Viagra to the same extent that it does a new drug for Tuberculosis (TB).

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[366] One may argue that from a strict utilitarian point of view, the investment of substantial resources for the treatment of rare conditions is not likely to maximize society's benefits. On the other hand, it may also be argued that the society has a moral obligation towards individuals who have had the misfortune of being affected by such a condition. Pieter Stolk et al., *"Rare essentials": Drugs for rare diseases as Essential Medicines*, 84 (9) BULL. WORLD HEALTH ORGAN (2006), *available at* http://www.scielosp.org/scielo.php?pid=S0042-96862006000900018&script=sci_arttext (last visited Sept. 30, 2011); *see also* C.A. Gericke et al., *Ethical issues in funding Orphan Drug Research and Development*, 31 J. MED. ETHICS 164 (2005).

[367] *See* Sudhir Anand & Kara Hanson, *Disability Adjusted Life Years: A Critical Review*, 16 J. HEALTH ECON. 685, 689-90 (1997).

[368] *See* C.J.L. MURRAY & A.D. LOPEZ, *'Rethinking DALYs'*, *in* THE GLOBAL BURDEN OF DISEASE: A COMPREHENSIVE ASSESSMENT OF MORTALITY AND DISABILITY FOR DISEASES, INJURIES AND RISK FACTORS IN 1990 AND PROJECTED TO 2020 20 (1996).

[369] *See* William Fisher & Talha Syed, *Global Justice in Healthcare: Developing Drugs for the Developing World*, 40 UNIV. CAL. DAVIS 581, 618 (2007).

The DALY and QALY frameworks need to be continually improved to address their various shortcomings. In particular, the measurement of various health states needs to be refined, as most such scores hinge on an accurate measurement of a particular health state and the effect of a drug in improving it.[370] Further, one must also evolve a sophisticated methodology of age weighting and discounting.

Lastly, the models ought to be adapted, to cater equitably to orphan diseases and to ensure that the prospects of drug discovery for such diseases are adequately incentivised. Towards this end, this thesis advocates that for the purpose of computing the extent of investment protection owed to a drug, the health impact of the drug be computed on a per patient basis and not on the basis of overall patient populations. It is likely that the impact may vary from country to country depending on the racial and genetic profile of patients.

Given that the DALY/QALY framework is coming to be adopted by more countries and institutions each year[371] (, I recommend the use of this, despite the

[370] *See* EuroQol, *How to Obtain EQ-5D*, http://www.euroqol.org/eq-5d/how-to-obtain-eq-5d.html (last visited Sept. 30, 2011) (noting that this is made difficult by the fact that lot of the data on QALY "health states" is not available because the EQ-5D database is protected and not in public domain).

[371] *See* Matthew D. Adler, *QALYs and Policy Evaluation: a New Perspective*, VI(1) YALE J. HEALTH POL'Y, L. ETHICS 1, 4 (2006) (noting the shift from the usage of QALY as a purely academic tool to one that is used by regulatory agencies: "The FDA, over the last half-decade or so, has repeatedly relied on QALYs in its rulemakings, pioneering a new approach to QALY-based analysis"). The United Nations World Health Organization has adopted the use of DALYs in calculating cost-effectiveness estimates, *See for e.g.* WHO, *Burden of disease and cost-effectiveness estimates*, http://www.who.int/water_sanitation_health/diseases/burden/en/index.html (last visited: Sept. 7, 2012).

various computation problems with such metrics. It is likely that an increase in the frequency of usage of the DALY/QALY framework in a variety of contexts, such as the proposed investment protection regime or the health impact fund (hereinafter "HIF") model discussed in Chapter VIII, will ensure that these frameworks evolve into a more nuanced format in the years to come.

### E. An International Regime

A purely national model of investment protection is one where the costs of the new drug are computed separately for each country and an exclusive period of protection is guaranteed in each country until such time that the profits earned in that country equal the costs incurred. However, such a national model of investment protection is largely arbitrary, as explained below.

Firstly, it is illogical to apportion the entire costs of drug discovery and development to a single country, merely because the drug regulatory approval was first obtained in that country. Most drugs are developed for global markets and it is only fair that the costs be apportioned between the various countries. This would mean that any meaningful investment protection regime must have a significant international component and cannot operate in isolation, at the national level.

I propose an international regime where the total global costs of drug discovery and development for any new drug, including the costs of all regulatory approvals are computed annually and apportioned between the various countries, depending upon the market share of the new drug in each country. This is further elaborated upon below:

Let us assume that "*X*", a drug originator, obtains its first regulatory approval for a new drug in the U.S. The total costs of drug discovery and development for the drug up to its time of approval is U.S. $500. The additional cost of obtaining approval in Europe is U.S. $200 and in Japan, U.S. $100. Under the model proposed in this thesis, *X* is to recover this amount (U.S. $800), as also a rate of return on investment corresponding to the average bank rate, and additionally, a rate of return on investment commensurate with the health impact of the drug. Let us assume that these rates of return add up to 25%. Therefore, the investment protection regime would need to work until *X* makes U.S. $1,000 (U.S. $800 + the 25% rate of return).

Assume that *X* earns revenue of U.S. $100 from the sale of the new drug in the US in a certain year. Let us label this as *X(ru)*. *X* earns U.S. $50 for a similar time frame in Europe *(X(re))* and U.S. $50 in Japan *(X(rj))*. The total worldwide revenues for that year are, therefore, U.S. $200. We now apportion the costs of drug discovery and development between the different countries, depending upon the proportion of sales of the drug in each country for that year. Thus, the proportion of

the costs that the U.S. has to bear is 50% (100/200) i.e. U.S. $500. Similarly, Europe and Japan would each have to bear 25% of the costs i.e. U.S. $250 each. The investment protection regime would operate in each of these countries in such a way that the period of exclusivity lasts till such time as the costs specific to that country are recovered.

It bears noting that the health impact of new drugs is likely to vary from country to country, depending upon the racial and genetic profile of patients.[372] Therefore, one has to take into account the average of the total health impact value for all countries where the drug is sold in a particular year. States can either insist on a local determination of health impact (in cases the where national authorities are vested with the power to make such determinations) or rely on such determinations from other countries. Further, the health impact value may change with time, as more information on the drug and its impact on patients emerge. The health impact value of the drug ought to, therefore, be revised from year to year.

An alternative is to constitute a global agency, which is tasked with assessing the average of the total health value and refining it year after year as more information on the drug becomes available. Such an agency could also be required to collate information on the costs and income of drugs annually. In this

[372] As noted earlier, the health impact of drugs under the proposed regime ought to be computed per patient and not in a manner commensurate with the size of patient populations, in order to avoid any potential prejudice to orphan drugs.

connection, it bears noting that the costs associated with drug discovery and development are also subject to variation each year, depending on the pursuit of new drug regulatory approvals in additional countries. Such costs associated with new drug regulatory applications ought to constitute a part of the total drug development costs. Further, the drug originator may also conduct additional trials in such countries to obtain regulatory approval. Therefore, the costs of the new drug ought to be re-calculated every year.

### F. Operation of Exclusivity

Unlike standard data exclusivity regimes, the market exclusivity granted by the proposed investment protection regime is not tied-in to regulatory data in any way. It offers absolute protection against all free-riders, of such nature that no competitors can enter the market with similar drugs, even if they have the resources to repeat clinical trials and generate their own data. To this extent, the model recommended is similar to the exclusivity associated with orphan drugs.[373]

Complete "market exclusivity", as opposed to mere "data exclusivity" means that no follow-on manufacturer can make or sell a drug containing an active ingredient that is similar to the one under protection. However, the issue of

[373] *See generally* Orphan Drugs Act, 1983. (Unlike other types of exclusivities for new drugs, as regards orphan drugs, the law provides complete market exclusivity for a 7 year period, thereby, preventing a competitor from entering the market, even if it were able to generate its own data); *see also* Eisenberg, *supra* note 20, at 359-61.

"similarity" can be a highly contentious one, particularly in the context of biologics, where even a small change in protein structure can have a significant bearing on efficacy and toxicity.[374]

Consider the facts of *Genentech v. Bowen*,[375] where Genentech was awarded orphan drug exclusivity for its drug, Protropin, used to treat children with a rare growth hormone related deficiency. The drug contained Human Growth Hormone (hGH), a protein obtained through genetic engineering processes involving the insertion of the human gene coding for this hormone into E. *coli* bacteria that rapidly multiplied and produced the hormone in large quantities. It was a significant improvement over the earlier hGH obtained from the pituitary glands of human cadavers, which was likely to contain a pathogen that caused Creutzfeldt-Jakob Disease in some patients. The Genentech recombinant hGH (r-hGH) drug, commercially marketed as "Protropin" had the same sequence of 191 amino acids found in pituitary derived hGH, with an additional methionine amino acid group attached to one end of the molecule. In other words, the Genentech product included an amino acid group not commonly found in the pituitary-derived hGH.

On December 12, 1985, the FDA designated Protropin as an orphan drug, thus, granting Genentech marketing exclusivity until December 12, 1992. Later, Eli

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[374] *See* Joseph A. Levitt & John V. Kelsey, *The Orphan Drug Regulations and Related Issues*, 48 FOOD & DRUG L. J. 525, 527 (1993).

[375] *See* Genentech, Inc. v. Bowen, 676 F. Supp. 301, 307 (D.D.C. 1987).

Lilly developed a similar hGH drug (Humatrope) and applied to the FDA for approval. Unlike Genentech's r-hGH product, the chemical structure of Lilly's product is identical to that of natural, pituitary-derived hGH; i.e., Lilly's drug does not contain the additional methionyl group found in Protropin. Genentech filed a "citizen petition" before the FDA arguing that for the purposes of the ODA, Lilly's drug was the same as Protropin and, therefore, ineligible for marketing approval until 1992.

However, the FDA ruled that Lilly's Humatrope was not the "same" under the ODA.[376] The District court upheld the FDA's determination,[377] despite the fact that, from a medical and clinical standpoint, there was no difference in safety and efficacy between Genentech's Protropin and Lilly's Humatrope.[378] The ruling was, therefore, sharply criticized by many as threatening to undermine the ODA's promise of market exclusivity; in such a legal environment a free-rider could simply execute a cosmetic change to an existing molecule for an approved orphan drug and thwart the originators' exclusivity.[379]

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[376] *See* Patricia J. Kenney, *The Orphan Drug Act--Is it a Barrier to Innovation? Does it Create Unintended Windfalls?*, 43 FOOD DRUG COSM. L. J. 667 (1988).

[377] *See* Genentech, Inc., *supra* note 375.

[378] *See* Novo Nordisk of N. Am., Inc. v. Genentech, Inc., No. 94 Civ. 8634 (CBM), 1995 WL 512171, at *18 (S.D.N.Y. Aug. 28, 1995), vacated, 77 F.3d 1364 (Fed. Cir. 1996); *see also* Robert A. Bohrer & John T. Prince, *A Tale of Two Proteins: The FDA's Uncertain Interpretation of the Orphan Drug Act*, 12 HARV. J. L. & TECH. 365 (1999).

[379] *See* Eller, *supra* note 289; *see also* David D. Rohde, *The Orphan Drug Act: An Engine of Innovation at What Cost?*, 55 FOOD & DRUG L. J. 125, 134 (2000).

The FDA later promulgated guidelines to suggest that a follow-on molecule would be considered "different", if it showed itself to be "clinically superior" to the known version under ODA protection.[380] Clinical superiority is defined as "a significant therapeutic advantage over and above that provided by an approved orphan drug …"[381] Therapeutic advantage[382] can be demonstrated in one of three ways: (1) greater effectiveness; (2) greater safety; or (3) a demonstration that the drug makes a major contribution to patient care in "unusual cases."

To prove greater effectiveness, the same kind of evidence is needed as that required to support a comparative effectiveness claim for two different drugs; i.e., an improvement as assessed by the drug's "effect on a clinically meaningful endpoint in adequate and well controlled clinical trials."[383] To support a claim of superior safety, the company seeking approval of the second product must establish that its product provides "greater safety in a substantial portion of the target populations, for example, by the elimination of an ingredient or contaminant that is associated with relatively frequent adverse effects."[384] Finally, a second drug

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[380] *See* Orphan Drug Regulations, 57 Fed. Reg. 62,076, 62,081 (1992) at 62,078. ("With regard to macromolecular drugs, clinical superiority by itself will render a subsequent drug different."); *see also* Levitt & Kelsey, *supra* note 374, at 528-29 (noting that this "clinical differences" standard was based on the principle that the market exclusivity should not create a barrier to needed patient therapies).

[381] *See* Orphan Drug Regulations, *supra* note 380, at 62,086.

[382] The terms therapeutic advantage and clinical superiority are interchangeable. Therapeutic advantage is demonstrated when clinical testing of a drug demonstrates it to be superior in an important dimension. 21 C.F.R. §. 316.3 (b) (3) (iii) (1999).

[383] 21 C.F.R. §. 316.3 (b) (3) (i) (1999).

[384] 21 C.F.R. §. 316.3 (b) (3) (ii) (1999).

can be considered "clinically superior" if it makes a “major contribution to patient care” such as, “the development of an oral dosage form where . . . only a parenteral dosage form’ had existed previously.”[385]

Much in line with the above, it is proposed, that under the investment protection regime advocated in this thesis, “newness” (or “sameness”) be construed such that only a significant difference in therapeutic efficacy of a later structurally similar drug would cause it to be treated as “different” from the originator drug and consequently it fall outside the scope of the granted exclusivity.

### G. Potential Abuse of Monopoly

As with all market exclusivities, the key disadvantage of a standard exclusivity-based investment protection regime is that it is likely to subject the market to the dictates of a single firm. This, in turn, it is likely to engender high monopoly prices, deadweight losses and consequent loss of consumer welfare.[386]

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[385] *See* 21 C.F.R. §. 316.3 (b) (3) (iii) (1999).

[386] *See* WILLIAM M. LANDES & RICHARD A. POSNER, THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW 17-20 (2003) (explaining that deadweight losses occurs when a seller with market power prices a product higher than the competitive price, which prevents some consumers from purchasing the product who otherwise would have done in a competitive market); *see also* F. M. Scherer, *A Note on Global Welfare in Pharmaceutical Patenting*, 27 WORLD ECON. 1127, 1141 (2004) (Deadweight loss is generally used to refer to circumstances where consumers cannot afford patented prices are forced to wait for the patent to expire. Such loss is especially troubling in the context of pharmaceuticals, since some patients must forgo the use of drugs that would improve their health and sometimes even save their lives).

A recent example is "Makena", a drug used to reduce the risk of pre-term births and which is based on an existing form of a hormone (progesterone), titled "17P". The said hormone had been available for many years for an average price of U.S. $10 from compounding pharmacies, which produced individual batches. KV Pharmaceuticals conducted trials on the drug, obtained FDA approval and began marketing it as Makena. It claimed that the trials were necessitated owing to apprehensions of purity and the consistency in the quality of the drug obtained through compounding pharmacies. The approval of Makena gave KV Pharmaceuticals 7 years of exclusive rights under the ODA, subsequent to which it priced the drug at about U.S. $1,500 per shot; an increase of 14,900%, when compared with the equivalent drug obtained from compounding pharmacies.[387] The pharmaceutical company also issued "cease and desist" letters to pharmacies, warning them that they could no longer sell their versions of drug.[388] In the wake of widespread protests against such price gouging, the FDA clarified that it "does not intend to take enforcement action against pharmacies that compound 17P, in order to support access to this important drug."[389]

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[387] *See* Tracy Staton, *Senators demand FTC probe of KV's Makena Pricing* (Mar. 21, 2011), *available at* http://www.fiercepharma.com/story/senators-demand-ftc-probe-kvs-makena-pricing/2011-03-21#ixzz1Jg9U25dc (last visited Sept. 30, 2011) (arguing that given that the drug has to be injected every week for about 20 weeks, the effective price burden on patients was likely to be a significant U.S. $30,000.)

[388] *See supra* note 296.

[389] As the FDA states on its website:

> FDA understands that the manufacturer of Makena, KV Pharmaceuticals, has sent letters to pharmacists indicating that FDA will no longer exercise enforcement discretion with regard to compounded versions of Makena. This is not correct. In order to support access to this important drug, at this time and under this unique

A similar case involved the plant-based drug "Colchicine," commonly known to cure gout and widely available for use at prices as low as U.S. $0.09.[390] URL Pharmaceuticals, a U.S. based pharmaceutical firm, tested Colchicine through clinical trials and obtained FDA approval in 2009, subsequent to which it was granted a 3 year marketing exclusivity for the treatment of gout[391] and a 7 year marketing exclusivity under the ODA for its use in the treatment of familial Mediterranean fever.[392] Thereafter, it priced the drug at U.S. $4.85 per pill, more than 4,000% of the prevailing price for the existing (albeit unapproved) versions in the market.[393] It also immediately issued legal notices to all other sellers of this drug, in effect forcing them off the market.[394] The above cases highlight the potential of market exclusivities to cause sharp and often unaffordable spikes in the

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> situation, FDA does not intend to take enforcement action against pharmacies that compound hydroxyprogesterone caproate based on a valid prescription for an individually identified patient unless the compounded products are unsafe, of substandard quality, or are not being compounded in accordance with appropriate standards for compounding sterile products. As always, FDA may at any time revisit a decision to exercise enforcement discretion.

*Id*.; *see also* US FDA, *FDA Statement on Makena* (March 30, 2011), http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm249025.htm.

[390] *See* Aaron S. Kesselheim & Daniel H. Solomon, *Incentives for Drug Development — The Curious Case of Colchicine*, 362(22) N. ENG. J. MED. 2045 (2010). ("The plant from which colchicine is derived was first used as a therapeutic agent for gout more than 3000 years ago in ancient Greece.")

[391] *See* Arthur Allen, *A Giant Pain in the Wallet*, http://www.slate.com/id/2289616/ (last visited Mar. 29, 2011).

[392] *See id*.

[393] *See* Kesselheim & Solomon, *supra* note 390 (stating that according to the Centers for Medicare and Medicaid Services, State Medicaid Programs filled about 100,000 prescriptions of colchicine in 2007 and paid approximately U.S. $1 million for the drug; use of the new version of colchicine from URL Pharmaceuticals was expected to add as much as U.S. $50 million per year to these insurance programs' budgets.)

[394] *See id*.

prices of pharmaceutical drugs, impacting public health and even human life in some cases.

Apart from this, market exclusivities raise the risk of an undersupplied market. Illustratively, during the bird flu outbreak, apprehensions were raised about Roche's ability to adequately supply the Tamiflu vaccine to all parts of the world which required it.[395] Roche initially protested any attempts to bring in other suppliers, and expressed its intention to remain the sole producer of Tamiflu.[396] Subsequently, owing to widespread protests and threats of compulsory licensing, Roche committed, in principle, to a wide licensing scheme so as to facilitate adequate and timely supplies in the event of a likely pandemic.[397]

### H. Compulsory Licensing

Since compulsory licenses are powerful *ex post* tools that engender more competition, increase supplies and reduce prices; an investment protection regime with an inbuilt compulsory licensing model is preferable to a pure market exclusivity model. One might also consider price controls as a valuable *ex post facto*

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[395] *See* Shamnad Basheer & Tahir Amin, *Taming of the flu: Working through the Tamilflu Patents in India*,1 J. INTELL. PROP. RTS. 113 (2006) (noting that Roche was the exclusive licensee of Gilead which owned the patent covering "Oseltamivir").

[396] *Id.*

[397] Roche entered into a manufacturing agreement with an India generic drug manufacturer, Hetero in order to meet the world-wide demand for the drug. *Roche sub-licences Tamiflu to Hetero Drugs*, FINANCIAL EXPRESS, Dec. 24, 2005.

tool to address the threat of excessive pricing. However, such controls may have fewer advantages when compared with a robust compulsory licensing scheme. For one, unlike a price control regime which has to necessarily fix an appropriate price for the drug in question, a compulsory licensing scheme could leave it to follow-on competitors to enter the market and drive down prices to more affordable levels.

Secondly, a drug originator that is averse to a "controlled" price could simply opt out of the market and, thereby, cause great harm to patients requiring the drug. Under a compulsory licensing regime, however, follow-on competitors can manufacture and sell the drug irrespective of whether or not the drug originator is itself operating in the market.[398] Thirdly, a compulsory licensing regime enables generic manufacturers to acquire further technological proficiency by offering them the freedom to legally copy a wider range of drugs. Fourthly, multiple follow-on drug manufactures ensure that the market does not suffer an under-supply problem, which might be the case if a market is subject to the whims of only one manufacturer, protected through a legally conferred monopoly.[399]

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[398] *See* Jean O. Lanjouw, *Intellectual Property and the Availability of Pharmaceuticals in Poor Countries, in* INNOVATION POLICY AND THE ECONOMY, Volume 3, 112-115 (Adam B. Jaffe, Josh Lerner & Scott Stern eds., 2003), *available at* http://www.nber.org/chapters/c10794 (criticising the use of a price control regime rather than competition to lower prices of drugs since patentees retain control over sales of pharmaceutical products and if prices are deemed to be too low, they could keep the products off the market or delay launching the product in a particular market; a compulsory licensing regime, on the other hand, in order to allow competition to reduce prices avoids the problems of long drawn–out negotiations over the controlled price levels.)

[399] *See supra* text accompanying notes 395-397 (discussing the Roche and Tamiflu case); *see also* Cole M. Fauver, Comment, *Compulsory Licensing in the United States: An Idea Whose Time Has Come*, 8 NW. J. INT'L L. & BUS. 666, 668-674 (1988) (arguing that a compulsory licensing regime in the U.S. can be justified on the grounds of "adequacy of supply," since the patentee, being a monopolist, would intentionally undersupply goods in order to maximize profits and granting a

When considering compulsory licensing, there are two alternatives. One could formulate a compulsory licensing regime based on specific grounds, largely in accordance with the framework of most patent regimes today. Illustratively, § 84 of the Indian Patents Act, 1970 stipulates that a compulsory licence could be granted if the patentee does not offer the patented product at a reasonably affordable price or does not ensure adequate supplies of the product in the market.[400] Alternatively, countries may wish to provide for a "groundless" compulsory licensing or compensatory liability regime, where no market exclusivity is granted in favour of the drug originator, but there merely exits a right to demand adequate compensation from follow-on entrants. The term "groundless" is a shorthand expression for a compulsory licensing scheme available as a matter of right to an interested party, without any need to demonstrate the existence of specific grounds such as excessive pricing by the drug originator.

The thesis proposes both alternatives, without expressing any strong preference one way or the other. It leaves it to states to make this determination depending on their national technological capabilities and preferences. Developing countries with a reasonably strong generic industry, such as India, may wish to activate a groundless compensatory liability model, since such a regime helps boost

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license to a competitor would enable meeting the leftover demand); *see also* Brian T. Liberis, *Compulsory Licensing and the TRIPS Agreement: A Solution to the High Drug Prices in the United States?*, 28 SUFFOLK TRANSNAT'L L. REV. 57, 76-77 (2004)

[400] *See* §84 of the Indian Patents Act, 1970.

the competitiveness of its generic industry and ensures the availability of low cost drugs to its patients.[401]

Under a compulsory licensing or compensatory liability model, the originator gains some level of protection, as the market entry of follow-on manufacturers is not "free," but based on a compensation to be paid to the originator. Such a model provides fair protection to data originators, whilst at the same time preserving some amount of generic competition in the market, such that consumers are able to access drugs at relatively more affordable prices. Drug prices under such a model are expected to be higher, than what might have prevailed in a completely free market scenario with no barriers to entry, since generic manufacturers need to compensate the drug originator and will likely pass on such costs to the consumer. Further, determining an appropriate quantum of compensation will entail administrative costs.

I use the term compulsory licensing to refer to a regime where follow-on innovators can enter the market only upon the occurrence of certain specified grounds (such as lack of adequate supplies or excessive pricing by the drug originator) and compensatory liability to refer to a more broad based framework,

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[401] *See* Shamnad Basheer & Annalisa Primi, *The WIPO Development Agenda: Factoring in the "Technologically Proficient" Developing Countries* (Oct. 19, 2008), http://ssrn.com/abstract=1289288.

where there is a complete lack of exclusivity in favour of the drug originator, but merely the right to claim compensation.

Whether one selects the first alternative (compulsory licensing triggered upon the existence of certain grounds) or a more broad based compensatory liability model that is near automatic in its operation, the key challenge is in determining the reasonable compensation to be paid by follow-on innovators. In the next section, I discuss existing models of compensation and then proceed to advocate what I believe to be a better methodology of compensation.

## I. Compensatory Liability and Computation Methodology

A compensatory liability regime is not a new idea, but has been proposed and implemented in different forms. I discuss the most prevalent models below and focus in particular on the compensation methodology. I subsequently discuss the shortcomings of existing models and recommend a better methodology of computing compensation.

### 1. Ethical Pathways Act

The Ethical Pathways Act[402] aims to avoid the duplication of clinical trials by permitting manufacturers of follow-on biologics (or biosimilars) to rely on the data

[402] *See* The Ethical Pathway Act, 2010 (US).

of the originator after paying a certain sum as compensation.[403] Under this Act, the Secretary is to establish a mechanism (known as an "ethical pathway") by which a follow-on applicant could request a cost-sharing arrangement with the originator.[404] Such an applicant has to first seek a voluntary licence from the data originator.[405]

If a voluntary agreement cannot be reached, parties are to submit to binding arbitration to determine a "reasonable" and "fair" licence fee for usage of data.[406] The arbitrator considers actual out-of-pocket costs of the clinical investigations, along with other factors such as R&D risks, federal grants, tax credits, expected share of the global market and the amount of time that the holder of the data has benefited from exclusive rights.[407] The Act seeks to engender more transparency in relation to the costs of innovation by requiring originators to provide sufficient information about the costs of the discovering and developing the drug and the compensatory amounts paid by follow-on manufacturers, and then making the information public.[408]

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[403] *See* James Love, *The Need for an Ethical Pathway* (November 2, 2010), *available at* http://www.keionline.org/misc-docs/biogenerics/kei2nov10fda.pdf.

[404] *See* The US Ethical Pathway Act, § 2(b), 2010.

[405] *See id.*, § 2(c)(1), 2010 (US).

[406] *See id.* § 2(c)(3)(B)(i), 2010 (US).

[407] *See id.*, § 2(d), 2010 (US).

[408] *See id.*, § 2(e), 2010 (US).

**2. FIFRA**

Under the US Federal Insecticide, Fungicide, and Rodenticide Act (hereinafter "FIFRA"),[409] pesticides with new active ingredients, registered after 1978, are granted a 10 year exclusivity period.[410] After this period, the data can be "relied" upon for the next 5 years by follow-on entrants who have to adequately compensate the pesticide originator.[411]

The compensatory amount has to be voluntarily agreed upon by the parties, failing which it is referred to arbitration.[412] The FIFRA does not set forth any explicit standard to compute "adequate remuneration;"[413] while some suggest that this ought to be "cost" based, other argue that it be "value" based.[414] A cost-based approach denotes an equitable sharing of the actual cost of producing test data. This sharing could be done on a per capita basis, where the costs are divided

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[409] *See* US Federal Insecticide, Fungicide, and Rodenticide Act, 7 U.S.C. § 136a3(c)(1)(F)(iii) (2000).

[410] *See id.* 7 U.S.C. § 3(c)(1)(F)(i) (2000).

[411] *See id.* 7 U.S.C. § 3(c)(1)(F)(i) (2000); *see also* Geoffrey H. Coll, *Determining Compensation for Subsequent Use of Test Data Under FIFRA: A value based or cost based standard?*, 11 COLUM, J. ENVTL. L. 193, 199 (1986).

[412] A follow-on applicant is to send the original data-submitter an offer to pay for use of the data. If at the end of ninety days after the date of delivery of the offer there is no agreement on the amount and terms of compensation, nor on a procedure for reaching such an agreement, then either party may initiate arbitration proceedings by requesting the Federal Mediation and Conciliation Service to appoint an arbitrator.

FIFRA § 136a(c)(l)(D)(ii) (1982).

[413] *See* FIFRA § 3(c)(1)(D)(ii) (1982). (As per this provision, the terms and amount of compensation may be fixed by agreement or failing such an agreement by binding arbitration.)

[414] *See* Coll, *supra* note 411, at 193.

equally between the originator and all subsequent follow-on entrants, or on a market share basis, where the costs are shared in a manner proportionate to the respective market share of follow-on entrants.[415]

Value based compensation, on the other hand, compensates an originator based on the "value" derived by a follow-on entrant who, by virtue of its reliance on the originator data, is able to enter the market at an earlier point in time. Such methodology is best exemplified in *Stauffer Chemical Co. v. PPG Industries*[416]**,** where, over and above awarding Stauffer (the originator of the pesticide) one-half of its direct aggregate testing cost (U.S. $1,465,000), the court also awarded a running royalty of ¢15 on every pound of Butylate (the protected active ingredient in question) sold by PPG from 1983 to 1992 (subject to certain adjustments).[417] The respondent, PPG, subsequently challenged the arbitral award on the ground that the compensation ought to have been based on a "cost" based methodology alone. The U.S. District Court for the District of Columbia disagreed, stating that no particular standard or formula is mandated under the statute, and that the arbitrators were free to consider any factors they deemed relevant.[418] In a subsequent decision, the arbitrator again relied on a "value" based methodology;

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[415] *See id.* at 194.

[416] *See* Stauffer Chemical Co. v. PPG Industries 16 199 077 82 Federal Mediation and Conciliation Service (1983); *see also* Coll, *supra* note 411.

[417] *See* Stauffer Chemical Co.*, supra* note 416; *see also* Alexander R. Nemajovsky, *Pesticides: Problems Facing the Industry in Submitting Proprietary Scientific Data to an International Organisation*, 19 GA. J. INT'L & COMP. L. 195, 207 (1989).

[418] *See* PPG Industries Incs v. Stauffer Chem Co., 637 F. Supp. 85 (1986) (U.S, District Court for the District of Columbia)

however, compensation granted to the originator was based on the follow-on registrant's highest market share during the first 5 years of its entry into the market.[419]

A commentator takes issue with this value based approach, arguing that:

> [t]he legislative histories of both the 1972 and 1978 amendments to FIFRA indicate that Congress intended that compensation be based on an equitable sharing of the costs of developing test data, rather than on the value of the data to a follow-on registrant. However, the legislative history is silent on the issue of how to equitably divide testing costs.[420]

The cost-based approach was adopted in *Cheminova v. Griffin*[421], where the arbitrator ordered the second market entrant (Griffin) to pay one-half of the costs of generating data incurred by Cheminivoa.[422] Griffin's argument, that it ought to pay a lesser percentage of the cost, since it had lower market share, was rejected by the arbitrator who held that market share was not relevant to the computation of compensation, since the follow-on entrant had an equal opportunity to compete in the same market.[423] The arbitrator opined that compensation based on a per capita allocation of costs reflected FIFRA's goals most appropriately.[424] The award was

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[419] *See* E.I. Du Pont de Nemours Co. v. Griffin Corp., 16 171 0080 86 American Arbitration Association (1988); *see also* Nemajovsky, *supra* note 417, at 208.

[420] *See* Coll, *supra* note 411.

[421] *See* Cheminova v. Griffin, 182 F.Supp.2d 68 (2002).

[422] *See* Nemajovsky, *supra* note 417.

[423] *See* Cheminova A/S, *supra* note 421 (discussing of details the arbitral award by the District Court).

[424] *See id.* at 182.

confirmed by the District Court.[425]

In a subsequent case,[426] an arbitral tribunal appeared to suggest that either a per capita basis or a market-share basis could be used to determine the appropriate compensation to be paid by follow-on entrants.[427] However, if market share were chosen as the determinant, it had to be based on the prospective market share (over a period of time long enough to amortize the cost of development of the originator pesticide) and consideration ought to be given to sales generated in the U.S. and other jurisdictions where the U.S. registration is sufficient to meet with regulatory requirements.[428] The tribunal also held that while computing the total costs of the originator to be compensated, the relevant interest rate and inflation ought to be taken into account.[429]

Given that a number of arbitral awards are not accessible to the public, one is unable to review such orders for a fuller account of the compensation methodology adopted. Even assuming that FIFRA computations were to be based on a clear "cost sharing" model, a simplistic per capita model would be far from optimal. Firstly, follow-on generic entrants may not have deep pockets to share the

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[425] *See id.*

[426] *See* FIFRA, § 3(c)(2)(B) (1982).

[427] *See* FMC Corp. v. Tricon Int'l, 16 199 0033 84 G American Arbitration Ass'n (1985); *see also* Coll, *supra* note 411, at 221.

[428] *See* Coll, *supra* note 411, at 222.

[429] *See* FIFRA, § 3a(c)(2)(D) (1982).

entire costs of data generation upfront in the first year of entry. Secondly, the model does not admit of easy computation, when further follow-on entrants enter the market. Assume that "*A"* is the originator and "*B"* is the first generic or follow-on entrant who pays 50% in the first year of entry. If a subsequent competitor, "*C"*, enters the market in the second year, would all parties have to now pay 33.3%? And would *A* have to return 16.6% to *B*? Thirdly, the percentage of costs to be paid by each generic entrant ought to have some co-relation with the benefits of market access. In other words, generic entrants ought to share only to the extent of their respective market shares.

**3. Fellmeth Model**

Aaron Fellmeth advocates a sophisticated cost-sharing model in the form of "readjustable royalties."[430] As the name suggests, the royalties to be paid by each generic entrant (labeled as "subsequent applicant" by Fellmeth) depends upon the total number of applicants each year and it varies (readjusts) each year upon the entry of new players.

Given that the first generic entrant enjoys the potential for maximal market access (compared with other subsequent entrants), Fellmeth proposes that this first-mover should pay the highest proportion of costs (computed as a percentage of the total originator costs), which can be fixed at any given percentage. Similarly,

[430] *See* Fellmeth, *supra* note 42, at 482.

the first few entrants who enter the market would have to pay more than those that enter the market in the later years and enjoy a correspondingly lower market access. In order to compute the precise percentage of compensation that subsequent entrants have to pay, Fellmeth proposes a formula as below:[431]

$$g = [a + 0.01(b-1)]/b$$

where '*g*' is the annual percentage to be paid by each subsequent applicant; '*a*' is the fixed annual percentage to be paid by the first subsequent registrant and '*b*' represents the total number of registrants.

The percentage amount recovered by the originator would be:

$$t = bge$$

where '*t*' is the originator's recovery and '*e*' is the duration of protection expressed in years.

While the Fellmeth model is certainly an improvement over the simple equitable cost division model,[432] it suffers from certain serious drawbacks.

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[431] *See* Razvan Dinca, *The Bermuda Triangle of Pharmaceutical Law-Is Data Protection a Lost Ship*, 8(4) J. W. INTEL. PROP. 517, 555 (2005).

[432] *See* Fellmeth, *supra* note 42, at 482 (referring to this as the simple division royalties model).

Firstly, it assumes that the first few entrants would have more access than subsequent ones. It could well be the case that subsequent entrants capture more of the market than earlier ones. Further, even with respect to follow-on firms which enter the market at the same time, some may capture a higher percentage of the market than others.

Secondly, the Fellmeth model stipulates an arbitrary percentage to be paid by the first generic entrant.[433] Dinca takes issue with the Fellmeth model for the above reasons.[434] He demonstrates that despite Fellmeth's promise, subsequent generic entrants could end up paying more than the first entrant. Dinca hypothetically fixes the percentage of compensation that the first generic applicant has to pay at 0.5 and shows that the second applicant in the second year ends up paying a higher figure than the first applicant in the first year. Thirdly, the Fellmeth model arbitrarily caps the total number of generic entrants that could enter the market prior to the compensatory period running out.[435]

**4. Dinca Model**

[433] *See* Dinca, *supra* note 431, at 557.

[434] *See id.*

[435] *See id*.

In order to address the various deficiencies in the Fellmeth model, Dinca proposes that compensation be computed as under:[436]

$$s = [C(1+i)]/[t(n+1)]$$

where, '*s*' is the compensation paid by each generic entrant, '*C*' the total costs incurred by the originator in creating the data, '*i*' the average banking interest rate for the year, '*t*' the number of years in the protection period and '*n*' the number of generic applicants who wish to use the data that year. The compensation received by the originator in a particular year would be '*ns*' i.e. the product of the number of generic applicants and the compensation to be paid by each such applicant.[437]

The following example is illustrative. Assume that the cost incurred by an originator "*O*" in generating regulatory data is U.S. $100 and the period of protection under the national law is 5 years. The average bank rate is 10% per annum. The compensation to be paid out by the first generic entrant "*A*" who wishes to rely on originator data, and enter the market in the year following the year in which the drug is first introduced by the originator would be:

$$s = [C(1+i)]/[t(n+1)] = 100(1 + 10/100)/5x2 = 11$$

[436] *See id*.

[437] *See* Dinca, *supra* note 431, at 558.

Let us now assume that two more generic applicants ("*B"* and "*C"*) wish to enter the market a year after *A*'s entry. The compensation that each such subsequent entrant ought to pay is as below:

*s = 100x1.1/5x4= 5.5*

At the end of 5 years of operating the model, the costs paid out by each generic entrant would be as below:

*A = U.S. $27.5 (U.S. $11 + U.S. $16.5 (U.S. $5.5x3 years)*

*B = U.S. $16.5*

*C = U.S. $16.5*

The contributions would add up to a total of U.S. $60.5. The originator would, therefore, have to bear U.S. $39.5 of the total cost of U.S. $100.

While Dinca's model is an improvement over the Fellmeth model, it suffers from the following drawbacks:

(a)It assigns an arbitrary time value in that Dinca suggests that the model should compensate for '*t*' number of years, without elaborating on why '*t*' was selected in the first place.[438]

(b)Much like Fellmeth, Dinca appears to consider only clinical trial costs as the relevant costs that count towards compensation. As has been repeatedly noted in this thesis, given the intensive nature of investments and risks associated with each stage of drug discovery and development, a comprehensive investment protection model ought to consider costs associated with the upstream drug discovery phase as well.

(c)As with Fellmeth, Dinca fails to consider the specific market share of the each follow-on generic entrant. Under his model, an entrant who captures only 10% of the market in a certain year would have to pay the same amount of compensation as another entrant who captures 50% of the market in that year.

## 5. Novel Methodology of Compensation

[438] *See* Dinca, *supra* note 431, at 560. ("In this model, the single element that should be settled by the legislator is the duration of protection.")

In order to provide for a more equitable solution than the models discussed above, I propose that follow-on market entrants pay an amount commensurate with their market share. Further, in order to ensure that the compensatory amounts paid out do not affect their bottom lines to a significant extent, I propose that they be made to pay only a certain proportion of their profits, and not their overall revenues. Lastly, the key advantage of this model is that it does not stipulate any arbitrary time period of protection. Rather, the model operates until such time as the costs along with a reasonable rate of return on investment are recovered by the drug originator.

Consider the hypothetical below, based significantly on the example cited in an earlier section of this Chapter dealing with the "exclusivity" based investment protection model. Assume that "*X*", a pharmaceutical originator firm obtains its first regulatory approval in the US on March 1, 2010. The total costs of drug discovery and development for the drug in question up to the time of approval in the U.S. is U.S. $800.

Under the proposed regime, *X* is to recover this amount, as also the normal bank rate of interest, and a rate of return on investment based on the health impact of the drug. Let us take the bank rate of interest to be the highest one prevailing in the year immediately preceding the one in which this model first operates. Let us assume that this is 10%. Let us also assume that the health impact of the drug merits a rate of return on investment of 15%. The total rate of return on investment

is, therefore, 25%. The compensatory liability model would need to work until *X* makes U.S. $1000 (800 + the 25% rate of return).

*X* earns a profit of U.S. $100 in the U.S. in the first year of the drug being sold (March 1, 2010 to Jan 1, 2011). Let us call this profit *X(p)*. A generic entrant "*Y*" also enters the market very close to *X*'s entry. *Y*'s profits *Y(p)* from the sale of the drug for that year is U.S. $50. We apportion the costs that *Y* would have to pay *X* in a manner proportionate to the market access of *Y* relative to *X*. We calculate market access on the basis of total revenues earned by each market entrant in a certain year. Let us assume that *Y* earns U.S. $100 and that *X* earns a revenue of U.S. $200 for the period above mentioned (Mar. 2010-Jan. 11). Given that *Y(r)* is one third of *(Y(r) + X (r))*, *Y* would have to pay one-third of its profits *Y(p)* for that year as compensation to *X* i.e. approximately US $16.67. We label this figure as *Y(c)*. If another generic entrant "*Z*" enters the next year, it would have to pay *Z(c)* to *X*, in accordance with the above formula.

However, we need to take into account *X*'s profits as well from the sales of the drug. Let us assume this is *X(p)*. Therefore, each year, the total compensation or cost recovery *(A)* flowing to *X* would be computed, thus:

$$A = X(p) + Y(c) + Z(c)$$

Once A reaches a sum of U.S. $1,000, the model stops operating and subsequently any firm is permitted to enter the market without paying any compensation whatsoever.

Since follow-on entrants are likely to commence their market operations at different times throughout the year, it is necessary to have a cut-off for computing the compensation due each year. Let us fix this cut-off as the first day of March each year. If a generic firm enters the market in January of a certain year, we compute the profits made up to the start of March and then compute the cost (in terms of its market share) that it needs to pay. Thus, if it makes only U.S. $10 in the 2 months since it entered and has a resulting market share of only 1%, it will have to pay 1% of its profits. However, for the purpose of ease of operation of the model, it could be stipulated that no follow-on entrant could enter the market after the 1st of February for that year. Competitors ought to make payments within a few months of the date of final computation. Assuming the administrative authority procures all relevant data and is able to arrive at the amount of compensation due by the start of April, firms can be asked to pay within the next 2-3 months.

**6. An International Regime**

The compensatory investment protection regime as discussed above is to work separately in each jurisdiction; such that only costs specific to that jurisdiction are considered and compensated for. However, as noted earlier, it is arbitrary to

attribute drug discovery and developmental costs to any particular country. An optimal regime is one that computes the global costs each year and then apportions them in a manner commensurate with market share of the drug in each country, as detailed below. To this extent, the proposed regime ought to be based on certain common international norms (relating to computation of costs and the like) that member states agree to implement domestically.

Assume that "*X*", a pharmaceutical originator firm obtains its first regulatory approval in the U.S. on March 1, 2009. The total costs of drug discovery and development for the drug in question up to this time of approval in the US is U.S. $500. The additional cost of obtaining approval in Europe is U.S. $200 and Japan, U.S. $100. Under the model proposed in this paper, *X* would recover this amount (U.S. $800), as also a rate of return on investment corresponding to the average bank rate and additionally, a rate of return on investment commensurate with the health impact of the drug. Let us assume that, as with the earlier example pertaining to the national model, this total percentage is determined to be 25%. Therefore, the compensatory liability model would need to work until *X* makes U.S. $1,000 (800 + the 25% rate of return).

Assume that *X* earns revenue of U.S. $100 in the U.S. in the first year of the drug being sold (March 1, 2009 - March 1, 2010). Let us label this as *X(ru)*. *X* earns U.S. $50 for a similar time frame in Europe *(X(re))* and U.S. $50 in Japan *(X(rj))*. The total worldwide revenues earned for that year are, therefore, U.S. $200. We now

apportion the costs of drug discovery and development between the different countries, depending upon the proportion of sales in each country for that year. Thus, the proportion of the costs that the US has to bear is 50% (100/200) i.e. U.S. $500. Similarly Europe and Japan would each have to bear 25% of the costs i.e. U.S. $250 each.

Once this relative national cost is computed, the model would operate in much the same way as earlier discussed. Assume that a generic entrant "*Y*" enters the U.S. market at a time very close to *X*'s entry. *Y*'s profits *Y(pu)* from the sale of the drug for that year in the U.S. is U.S. $50. We apportion the costs that *Y* would have to pay *X* in a manner proportionate to the market access of *Y* relative to *X*. Assuming that *Y(ru)* is one-third of *X(ru) + Y(ru)* (as from the earlier example), *Y* would ordinarily have to pay one-third of the total amount of its profits to *X* within the US. We label this figure as *Y(cu)*. It may then have to pay a different compensation amount in Europe and Japan (*Y(ce)* and *Y(cj)* respectively), depending on:

i) its date of entry into the Europe and Japanese markets

ii) the proportionate cost of drug approval in the Europe and Japan (computed as a proportion of *Y*'s revenues in Europe and Japan, relative to that of *X*); and

iii) the profits made by *Y* in the Europe and Japanese markets.

If another generic entrant "*Z*" enters that year, *Z* would pay *Z(cu)*, *Z(ce)* and *Z(cj)* assuming it enters all 3 markets.

Each year, the total compensatory amount *A* flowing to *X* is computed, thus:

$$A = X(pu + pe + pj) + Y(cu + ce + cj) + Z(cu + ce + cj)$$

This model continues year after year until *A* reaches U.S. $1,000. As noted in an earlier section dealing with the exclusivity based model, drug originator costs have to be recalculated each year, since it is possible that additional regulatory approvals are procured in new countries.

In conclusion, a compensatory liability model encourages more competition and drives down prices and is, therefore, more advantageous from a patient and public health perspective, when compared to a pure market exclusivity model. However, the key challenge is in working out a framework that is institutionally competent and cost efficient to administer.[439] I offer a model of compensation which avoids the shortcomings of earlier models and makes for a fair and logically sound assessment.

[439] *See* Mark A. Lemley & Philip J. Weiser, *Should Property or Liability Rules Govern Information,* 85 TEXAS L. REV. 783 (2007), (lamenting the fact that in all the debates about property versus liability rules, scholars often tend to ignore issues of institutional competence and costs).

## J. Electing between Patents and Investment Protection

The investment protection regime advocated in this Article compensates the drug originator comprehensively for expenses associated with drug discovery and development. Therefore, any additional patent protection for the drug originator over the same drug will lead to over-compensation. In order to reduce the scope for such over-compensation, it is recommended that the firm in question be forced to elect between the two regimes. If it chooses to retain its patent rights, it cannot avail of the proposed investment protection regime. Similarly, if it chooses to avail of the investment protection regime, it has to necessarily relinquish all patents covering the drug.[440]

The key advantage of the investment protection regime over the patent system is that the former guarantees some amount of market protection, either through exclusivity, compensatory liability or through a reimbursement from public funds or prizes. A patent on the other hand remains susceptible to uncertainty, as the patent could be invalidated at any time in most countries. It is also possible that courts refuse injunctions to restrain infringers, but simply award damages after a prolonged trial.

[440] However, such relinquishing will only operate in relation to similar versions of the drug that are protected under the investment protection model. In other words, the drug originator should be free to sue on the basis of its patent right, when the said patent is used in conjunction with an unrelated drug (a drug that is not same or similar to the initial drug under consideration, for which the investment protection model operates).

On the other hand, a patent regime is advantageous to drug originators in that they are saved the trouble of having to submit sensitive cost data. Further, in some cases (depending on the patent term remaining after the drug is approved and marketed), it could enable the originator to gain a longer period of protection than an investment protection regime.

The HIF (Health Impact Fund) model, elaborated upon in a later chapter[441] also advocates a similar election between the HIF fund and the patent system. As the authors of the model note, firms are likely to elect the HIF fund only when they expect greater returns from the fund, when compared with an unconstrained use of patent exclusivity.[442]

One might ask if the above election scheme is compatible with TRIPS. I argue that it is for the following reasons. Firstly, patents are not necessarily denied to a drug originator in violation of TRIPS. Rather, it is left up to the originators' discretion as to whether or not it wishes to forego this protection in favour of the investment protection regime.

While critiquing the current patent system and advocating for an incentive system based on prizes, Fisher and Syed express a similar view i.e. a voluntary prize

[441] *See infra* text accompanying notes 701-705

[442] When the payment per QALY drop too low, firms are likely to opt out of the HIF and prefer patents instead. *See* Hollis, *infra* note 701, at 129.

system that exists alongside the patent system is compatible with TRIPS as the drug originator is not denied patent protection but is choosing to eschew it in favour of the proposed prize model.[443]

In the *Indonesia Autos* case[444], which dealt with the legality of tax and import duty exemptions on cars that met certain requirements under the 'National Car Programme' (NCP), the United States claimed that Indonesia violated Article 20 of TRIPS.[445]

Under the programme, a trademark applicable to a 'national motor vehicle' i.e. a car that qualified for benefits under the programme had to be owned by an "Indonesian" company. The US argued that if its companies entered into an arrangement with a Pioneer company (a domestic company manufacturing cars eligible for benefits under the NCP), it would be unlikely to additionally use the trademark it used globally on the car marketed as a 'national motor vehicle' in order to avoid confusion resulting from the use of two marks on the same car.

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[443] *See* William W. Fisher , Talha Syed, *A prize system as a partial solution to the health crisis in the developing world*, 46 (Oct., 2008), *available at* http://www.law.berkeley.edu/files/Fisher_Prizes12.pdf,.

[444] Panel Report, *Indonesia- Certain Measures Affecting the Automobile Industry*, WT/DS54/R (Jul. 2, 1998) (*hereinafter* Indonesia Autos Panel Report)

[445] The US also argued its national treatment obligations under art. 3 of TRIPS, since the programme discriminated against nationals of other WTO member states in respect of acquisition and maintenance of trademarks.

To this extent, the US argued that since it would be 'encumbered' in using the trademark it normally used in other parts of the world, the Indonesian programme constituted a violation of Article 20 of TRIPS which required that "(t)he use of a trademark in the course of trade shall not be unjustifiably encumbered by special requirements, such as use with another trademark, use in a special form or use in a manner detrimental to its capability to distinguish the goods or services of one undertaking from those of other undertakings."

The Panel however rejected this argument on the basis of the voluntary nature of programme, noting that "if a foreign company enters into an arrangement with a Pioneer company, it would do so voluntarily, with knowledge of any consequent implications for its ability to maintain pre-existing trademark rights..."[446]

The above ruling suggests that a "voluntary" arrangement wherein a drug originator is asked to choose between a TRIPS mandated patent protection and an optional investment protection regime is not likely to violate Article 27 or any other provision of TRIPS.

[446] Indonesia Autos Panel Report, at ¶ 14.271. The US also argued that owing to its foregoing of the use of the global mark on cars manufactured for the Indonesian programme, the said global mark could be rendered susceptible to cancellation in Indonesia due to non-use. The panel however rejected this argument. *See* Indonesia Autos Panel Report, at ¶ 14.270.

### K. The Advantages of an Investment Protection Regime

When compared with a standard data exclusivity regime, the primary advantage of a comprehensive investment protection model is that it asks for the actual cost of discovery and development for each drug and grants proportionate protection based on this specific investment. The regime is premised on the logic that while the investment may be recouped in a mere 2 years for some drugs, it could take up to 7 years for others.

It is pertinent to note that drug discovery and development is conducted with the help of public funding in many cases.[447] Such funding must be deducted from the overall costs claimed, and the originator must not be permitted to lay claim to a period of exclusivity and recoup an amount disproportionate to what it actually contributed. A recent study demonstrates that public funded institutions have contributed to the discovery of 9.3% to 21.2% of all drugs involved in new drug applications from 1990 to 2007.[448] A similar study conducted earlier established that while the overall percentage of drugs that came out of university

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[447] *See* National Institute of Health (hereinafter "NIH"), *Biennial Report of the Director FY2008 & 2009- Clinical and Translational Research (2008)*, *available at* http://report.nih.gov/biennialreport/ViewSection.aspx?sid=18&cid=3 (last visited Sept. 30, 2011) (The NIH runs an NIH Clinical Trial Grant Program usually sponsoring a budget up to U.S. $100,000 of direct costs and sometimes upto U.S. $450,000 for every drug which it approves under the program.); *see generally* US Department of Health and Human Services, *Types of Grants Programs*, http://grants.nih.gov/grants/funding/funding_program.htm (last visited Sept. 30, 2011) .

[448] *See* Ashley J. Stevens et al., *The Role of Public Sector Research in the Discovery of Drugs and Vaccines*, 364 NEW ENG. J. MED. 535, 540-41 (2011).

research was relatively low (at 7.7%), the figure was substantially higher (19.2%) for the most innovative drugs, i.e. New Molecular Entities (NMEs).[449]

The second advantage of the proposed regime is in terms of its potential to disincentivise the creation of ever-greened or "me-too" drugs.[450] The term "ever-greening" is one that has healthy overtones in the environmental sciences[451] but is pejorative when applied to the pharmaceutical industry.[452] As yet, there is no standard definition for this term; rather, its popular usage often refers loosely to a set of practices designed to preserve market exclusivities by patenting derivatives which often confer little or no advantage to the patient, when compared with the previous parent drug.[453]

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[449] *See* Sampat, *supra* note 19 (stating that further, universities owned patents accounted for over one-quarter of HIV-AIDS drugs approved in the reference period).

[450] *See* BOLDRIN & LEVINE, *supra* note 56, at 226 (stating that only 25 to 30%of the total R&D expenditure goes towards new drugs, with the rest being utilized for the development of me-too drugs); *see also* Huskamp, *supra* note 9.

[451] Evergreen trees are present in areas where there is either no unfavourable period for growth, or the growing season is very short. MADHU ARORA, DICTIONARY OF BOTANY 123 (2nd ed., Rep. 2004). (explaining that the term "evergreen" is used for a woody perennial plant that is bearing and losing leaves continuously throughout the year). For more information, see PETER THOMAS, TREES: THEIR NATURAL HISTORY 28-29 (2000).

[452] A US congressional report which terms evergreening as 'a potentially perjorative term that generally refers to the strategy of obtaining multiple patents that cover different aspects of the same product, typically by obtaining patents on improved versions of existing products' For an interesting discussion see John R. Thomas, *Patent "Evergreening": Issues in Innovation and Competition,* Congressional Research Service (November 13, 2009), *available at* http://ipmall.info/hosted_resources/crs/R40917_091113.pdf. (noting that evergreening is: 'a potentially pejorative term that generally refers to the strategy of obtaining multiple patents that cover different aspects of the same product, typically by obtaining patents on improved versions of existing products.')

[453] *See* Whirlpool Corp. v. Camco Inc., [2000] 2 S.C.R. 1067, ¶ 37). (defininig ever-greening in the context of "double patenting" by noting that,'a patentee who can "evergreen" a single invention through successive patents by the expedient of obvious or uninventive additions prolongs its monopoly beyond what the public has agreed to pay.') For an interesting discussion see MACHLUP,

The *Prilosec vs. Nexium* example is a good illustration of this phenomenon. As Astra Zeneca's patent over its anti-heart burn drug, "Omeprazole" (brand name, Prilosec) expired, it introduced an allegedly superior derivative, "Esomeprazole" (brand name, Nexium).[454] The active ingredient underlying Nexium was the same as that of Prilosec, the key difference being that while Prilosec was a racemic mixture, Nexium was one of the enantiomers that constituted the racemic mixture.[455]

The investment protection model advocated in this thesis addresses the scourge of evergreening by stipulating that drugs merit a rate of return on investment proportionate to their health impact. If, as was the case with Nexium, the health impact of a drug is relatively insignificant when compared with its earlier known equivalent, it will merit only a miniscule rate of return on investment. Secondly, the costs associated with developing such an ever-greened variety are likely to be far lower than that associated with discovering and developing the first in time drug (Prilosec). Therefore, the period of exclusivity

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*supra* note 211, at 36-38 (discussing that the phenomenon of ever-greening dates back to at least the 1930s and citing to the 1939 TNEC Hearings, which discussed the patenting of minor improvements to continue protection of the original invention).

[454] *See* Neil Swidey, *The Costly Case of the Purple Pill*, BOSTON GLOBE MAGAZINE, November 17, 2002, http://home.comcast.net/~neilswidey/pill.htm (stating that Esomeprazole is the *S*-enantiomer of omeprazole (marketed as Losec/Prilosec), and AstraZeneca claims improved efficacy of this single enantiomer product over the racemic mixture of omeprazole. However, this alleged efficacy has been severely disputed.)

[455] *See* Gardiner Harris, *Prilosec's Maker Switches Users To Nexium, Thwarting Generics*, WALL ST. J. (June 6, 2002), http://www.chelationtherapyonline.com/technical/p36.htm.

associated with Nexium (even if approved by the regulator) is likely to be far lower than that associated with Prilosec. Thirdly, even assuming a Nexium-type variant with relatively insignificant health impact were to be developed by another drug manufacturer and not necessarily Astra Zeneca, the investment protection regime proposed in this thesis would disincentivise such creations, as they protect the originator molecule from pure generic versions, as also from versions that are not the same, but only "similar" to the originator molecule. It is hoped that all of the above will disincentivise the creation of ever-greened derivatives which have insignificant health impact. The evaluation of health impact (which in turn determines the rate of return on investment) has to be made by the drug regulatory agency or any other authority at the time of drug approval. However, as noted earlier, the health impact value will be recalibrated during the time of operation of the drug, in the light of new and emerging evidence.

Thirdly, a significant advantage of the investment protection regime in this thesis is that unlike existing data exclusivity regimes, it is not tied to regulatory data in any way. Rather, it includes the cost of regulatory data as well as upstream drug discovery investments. Fourthly, it provides a broader market exclusivity (than regular data exclusivity regimes), where a follow-on entrant cannot enter the market, even if it generates its own data. In other words, the drug originator can prevent any third party from entering the market, if such third party develops a drug or drug derivative that is not significantly clinically superior to that of the

drug originator. To this extent, the proposed regime goes beyond protecting the originator against mere free-riders.

In this context, it is important to appreciate that while data exclusivity regimes may be seen to have an "investment" inducing function, they are tied-in to the larger purpose of drug regulation, which is to ensure that drugs are safe and effective. To this extent, I propose that the investment protection models advocated in this thesis are better seen as a stand-alone investment protection regime, rather than as an amendment to any of the existing data exclusivity regimes. Such a comprehensive regime dispenses with the need to have a separate data exclusivity regime, barring special instances such as paediatric exclusivity, where additional trials on paediatric populations may need to be incentivised, after the drug has gained marking approval.[456]

Unlike patents, where an *ex ante* evaluation of the merits of a technology and a determination of an appropriate level of protection will prove difficult,[457] an investment protection regime is more amenable to such determination, as it requires individual costs and profits per drug. In order for the model to work, all drug companies that wish to benefit from this scheme ought to submit their costs of

[456] *See supra* text accompanying notes 250-252 for discussion on paediatric exclusivity.

[457] *See* Francesca Cornelli & Mark Schankerman, *Patent renewals and R&D Incentives*, 30(2) RAND J. ECON. 197, 209 (1999) (admitting that there is an inherent difficulty of valuing patent inventions at the stage of patenting while considering optimal patent duration and stating that rather inventors have to rely a lot on "post-patent" learning).

drug discovery and development (as well as their yearly profits) to the relevant body which would be tasked with implementing this model. Risks of costs inflation and manipulation exist, but as noted earlier, this is likely to abate over time as the model matures in its working. An incidental advantage of the proposed model is that, over a period of time, one is likely to get a more accurate estimate of the average costs for drug discovery and development. Given the general reluctance of pharmaceutical firms to share such figures, the proposed model will promote more transparency and prove tremendously valuable in the long run.

A question may arise in this context: would a model of cost reimbursement, where all costs of R&D are compensated, breed inefficiency? While considering the feasibility of opening up the non-obviousness or inventive step standard to consider the costs of innovation, Scotchmer notes that, "[e]vidence about costs would be even more problematic. Rewards should not be based on accounting cost, as that might reward inefficiency."[458]

While this concern may have some merit generally, in the specific context of an investment protection regime for pharmaceutical drugs, it may not be that significant. Such a regime would only reward successful drugs and it is difficult to know in advance as to which drugs are likely to be successful and merit approval from the FDA or other regulator. It is, therefore, unlikely that drug firms would

[458] *See* Scotchmer, *supra* note 215, at 10.

permit their process of R&D to lapse into inefficiencies that cost extra money, which may or may not be recoverable in the end.

While scholars have begun to expose the weaknesses of the patent system in promoting pharmaceutical innovation,[459] none of them propose a comprehensive investment protection regime as I have. Even those who focus on investment protection, advocate the use of the data exclusivity regime. This thesis demonstrates the limitations of the data exclusivity regime, most pertinent of which is that the protection is tied to the submission of regulatory data and it covers only costs relating to clinical trials. Further, it offers a uniform period of protection without regard to the specific amount of investment or the health impact of the drug. Lastly, the thesis proposes an inbuilt compulsory licensing mechanism or a broader compensatory liability model in order to provide against potential abuse of the monopoly by a drug originator, including excessive pricing and limited supplies. It advocates that follow-on innovators be permitted to enter the market upon the payment of reasonable compensation to the drug originator. It proposes a novel methodology of computing compensation, whereby a reasonable amount, which balances the interests of the interests of both the drug originator and the follow on innovator, is to be paid. The compensation methodology is tailored to take into account the global nature of pharmaceutical innovation and the various international markets which are exploited by a drug originator on a regular basis.

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[459] *See* Roin, *supra* note 2; *see also* Heled, *supra* note 193; *see also* Sichelman, *supra* note 98; *see also* Eller, *supra* note 289.

## L. Disadvantages of an Investment Protection Regime

The key disadvantage of an investment protection regime is that in seeking to determine the appropriate costs associated with drug discovery and development that merit compensation, the regime will entail significant administrative and implementation costs.

Given that the various accounting methodologies and costs associated with drug discovery and development remain contested to this day, the investment protection regime proposed in this Article is likely to witness some amount of cost exaggeration from drug originators[460]

Cost exaggeration through a variety of creative accounting techniques[461] have been deployed in a wide variety of instances – the most famous being the Enron accounting scandal where a leading global energy corporation deliberately misled the public about its profits by concealing its debts in the company's accounts.[462]

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[460] *See* Merges, *supra* note 214 (noting that, "firms try to characterize as many expenses as possible as R&D-related for purposes of the R&D tax credit," in the context of tax credits); *see also* J. Cordes, *A Survey of Research Findings on the R&D Tax Credit*, *in* THE R&D TAX CREDIT: ISSUES IN TAX POLICY AND INDUSTRIAL INNOVATION 5, 11 (Kenneth Brown ed., 1984).)

[461] Creative accounting is defined as a *"[f]orm of accounting which, while complying with all regulations and practices, nevertheless gives a biased impression (generally favourable) of an entity's financial performance and position." See* CHARTERED INSTITUTE OF MANAGEMENT ACCOUNTANTS, OFFICIAL TERMINOLOGY 64-65 (2005).

[462] *See* Samantha Thapa & Christopher L. Brown, *Corporate scandals, the Sarbanes-Oxley Act of 2002 and equity prices*, ACAD. ACCT. FIN. STUD. J. (Jan. 2007).

Such inflation has also been witnessed in relation to tax credits; a study conducted by the US Congressional budget office in relation to tax credits claimed by drug originators notes: "[t]o take advantage of the favorable tax treatment of spending for research and development, firms have an incentive to classify as many expenses as possible as R&D related, an incentive that grows with the credit's generosity."[463]

In order to reduce the prospects of cost exaggeration and overcompensation, an investment protection regime could include the following safeguards:

(a) All cost estimates that are submitted to the relevant government authority have to be made public.[464] This is likely to trigger objections from competitors and civil society members who may identify a deliberate inflation of costs or methodological flaws in the computation mechanism. In order to provide a more robust framework for such critique, one could devise a system similar to the patent opposition

[463] *See Federal Support for Research and Development,* CONGRESS OF THE UNITED STATES: CONGRESSIONAL BUDGET OFFICE, 24 (Jun. 2007), *available a*t http://www.cbo.gov/sites/default/files/cbofiles/ftpdocs/82xx/doc8221/06-18-research.pdf *; see also* Koh Jun, Ong*, Rare Diseases – a Sustainable Model for the Pharmaceutical Industry, available at* http://www.gsk.com/rare-diseases/papers/winner-3_koh-jun.pdf (last visited: Apr., 26, 2012) ("There is also a risk for companies to maximise tax claims by means of creative accounting." *Id.,* at 4).

[464] *See* Robert Weissman et al., *A Cost sharing model to protect investments in Pharmaceutical test data*, (CPTech Policy Brief No. 1, Apr.-May, 2006), *available at* http://www.cptech.org/publications/policybrief-no1-cost-sharing.pdf.

machinery, where third parties are invited to contest the computation through a speedy and inexpensive administrative process.[465]

(b) Costs could be made mandatorily auditable by an independent certified third party, in accordance with internationally accepted accounting norms.[466]

(c) Costs could also be verified against R&D costs that are likely to be submitted to other regulatory authorities such as tax returns or filings claiming tax credits. A number of countries around the world offer such tax credits as incentives for investment in R&D.[467] However this comes with the caveat that the figures submitted for tax credits themselves may be inflated as noted earlier.

(d) Lastly, one could also borrow from costing methodologies deployed in other legal regimes that seek to regulate the prices of drugs such as drug price regulations and competition law. Illustratively, in Belgium and Finland, the maximum price at which a drug can be sold is set with

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[465] *See* § 25(1) & (2), Indian Patents Act, 1970 (In India, for *e.g.*, a patent can be opposed by a third party on extensive grounds both before and after grant of the patent).

[466] *See* Fellmeth, *supra* note 42, at 495.

[467] Deloitte undertook a survey of R&D tax incentives in 25 countries. *See* Deloitte, *Global Survey of R&D Tax Incentives*, (2011) *available at* http://www.investinamericasfuture.org/PDFs/Global%20RD%20Survey%20Final%20-%202011.pdf (last visited: Apr. 30, 2012 ).

reference to a number of factors including research and development costs.[468]

Similarly, European competition authorities engage in cost determinations whilst determining whether an undertaking has abused its dominant position by engaging in excessive or predatory pricing.[469]

Notwithstanding the above safeguards, an objective determination of true costs will always prove difficult and contentious and likely involve significant operational costs. The objective of this article is not to yield a perfect model, if ever there was one;[470] rather, it is to advocate a regime that is at least relatively more optimal as an investment protection instrument than the current patent system, which is premised *inter alia* on a faulty uniform period of protection. Given that the patent regime seeks to foster innovation and creativity, it will be rather paradoxical if the regime itself were shielded from any innovative experimentation.

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[468] PHRMA, *Pharmaceutical Price Controls and other Market Access Barriers in Developed Countries*, , 5, 14 (2004), *available at* http://ita.doc.gov/td/health/phRMA/phRMA%20-%20ANNEX%20A.pdf (containing an overview of the price control regimes of various countries). *See* also Panos Kanavos, *Overview of Pharmaceutical Pricing Reimbursement Regulation in Europe*, LSE HEALTH & SOC. CARE (2001), 9, http://www.eco.uc3m.es/servicios/sesam/actividades/jornada_legislacion/DOC%209%20EMEARoadMap.pdf.

[469] *See* United Brands v Commission, [1978] 1 CMLR 429; CICCE v Commission [1985] ECR 1105. *See also The Supply of Banking Services by Clearing Banks to Small and Medium Sized Enterprises*, COMPETITION COMMISSION, 5319 (2002), a case concerning excessive pricing in the supply of banking services by clearing banks to small and medium sized enterprises.

[470] *See* Derek E. Bambauer, *The Myth of Perfection*, 2 WAKE FOREST L. REV. 22 (2012), *available at* http://wakeforestlawreview.com/wp-content/uploads/2012/04/Bambauer_Common-Law.pdf ."Scholars should cast out the myth of perfection, as Lucifer was cast out of heaven. In its place, we should adopt the more realistic, and helpful, conclusion that often good enough is . . . good enough". *Id.,* at 22.

One may argue that by pegging permissible rates of return and setting limits on the extent of profits that pharmaceutical firms may make, the proposed regime effectively converts the pharmaceutical sector to a public utility. Firstly, it is important to note that the regime does not set aim to set prices or regulate prices charged by the innovator. Rather, it simply ensures that there is market protection till such time as investments are recouped along with appropriate rates of return depending on the health impact of the drug. To this extent, it is somewhat different from other cases of public utilities such as electric power, telephones, oil and natural gas pipelines etc,[471] which are generally regulated by "granting of a franchise to a firm as the sole supplier and then setting prices, or rates, such that the firm can earn no more than a "fair" rate-of-return on its invested capital…"[472]

Secondly, the onset of rapidly escalating drug prices are causing governments to regulate the pharmaceutical sector more intensely,[473] taking it closer to a public

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[471] *See* HENRY G. GRABOWSKI & JOHN M. VERNON, THE IMPACT OF REGULATION ON INDUSTRIAL INNOVATION 33 (1979).

[472] *Id.*

[473] Marcia Angell, *The Truth About the Drug Companies*, 51 (12) N.Y. Rev. Books, 9 (Jul. 15, 2004), http://www.nybooks.com/articles/archives/2004/jul/15/the-truth-about-the-drug-companies/?pagination=false ("State governments, too, are looking for ways to cut their drug costs. Some state legislatures are drafting measures that would permit them to regulate prescription drug prices for state employees, Medicaid recipients, and the uninsured."); *see also* Kaiser Foundation, *Health Poll Report*, Jan./Feb. 2005, *available at* http://www.kff.org/healthpollreport/feb_2005/upload/full_report.pdf ("The public's concerns about prescription drug prices and drug company profits translate into support for many proposals to control drug costs. For example, in 2005, almost two-thirds (65%) of the public say there should be more government regulation of prescription drug prices, and 70% of these people (or 46% of all

utility. A number of countries have price control regimes in place to regulate excessive pricing by pharmaceutical firms.[474] Illustratively, the United Kingdom (through its Pharmaceutical Price Regulation Scheme) imposes a rate-of-return profit regulation common to public utilities, on the pharmaceutical industry.[475] The rationale behind such public utility style regulation is that, "monopoly firms … typically have government-granted monopolies through the patents they possess) should be required to charge the price that would prevail in a competitive market, which is equal to the efficient production costs and a rate of return on capital as would be determined in a competitive market."[476]

Much like other public utilities, the pharmaceutical sector is 'relatively capital intensive'.[477] Firms experience "a large time lag for approval and large sunk costs for R&D" making them "more akin to utilities rather than the majority of other Fortune 500 industries."[478]

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adults) continue to support more regulation of prices even it leads to less research and development of new drugs.")

[474] *See* F.M. Scherer, *The Pharmaceutical Industry – Prices and Progress*, 351(9) NEW ENG. J. MED. 927, 929 (2004) (citing P.M. DANZON, PHARMACEUTICAL PRICE REGULATION: NATIONAL POLICIES VERSUS GLOBAL INTERESTS (1997))

[475] *See* SEBASTIAN LINNEMAYR ET AL., RAND CORPORATION, NEGOTIATION STRATEGIES FOR ANTIRETROVIRAL DRUG PURCHASERS IN THE UNITED STATES 9 (2012) ("the British NHS limits a manufacturer's return on its business with the NHS to 20 percent.")

[476] *Id.,* at 10.

[477] *See* GRABOWSKI & VERNON, *supra* note 471, at 37.

[478] Jerry Stanton, Comment, *Lesson for United States from Foreign Price Controls on Pharmaceuticals*, 16 CONN. J. INT'L L. 149, 156 (2000-2001).

Scholars such as Marcia Angell therefore advocate that the drug industry be treated as a public utility:

> …drug companies are dependent on the public for a host of special favors—including the rights to NIH-funded research, long periods of market monopoly, and multiple tax breaks that almost guarantee a profit. Because of these special favors and the importance of its products to public health, as well as the fact that the government is a major purchaser of its products, the pharmaceutical industry should be regarded much as a public utility.[479]

Critics however take issue with this approach noting that increased intervention would inevitably stifle innovation.[480]Angell however responds by noting:

> Just as public utilities are not permitted to charge whatever the traffic will bear, neither should drug companies. It is hard to take seriously the inevitable industry argument that price controls would stifle innovation and frighten investors when profit margins are so great and so much revenue is spent on marketing.[481]

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[479] Angell,*supra* note 473, at 13

[480] *See for e.g.* Paul Roderick Gregory*, Obama Care Will End Drug Advances and Europe's Free Ride (Unless China Steps in)*, FORBES, Jan. 7, 2012, http://www.forbes.com/sites/paulroderickgregory/2012/07/01/obama-care-will-end-drug-advances-and-europes-free-ride-unless-china-steps-in/ ("Ultimately, Obama Care will turn our pharmaceutical industry into a quasi-public utility that earns a moderate federally-set profit by churning out established drugs. The risk-averse FDA will still insist on a rigorous approval process, meaning that the costs and risks of new drug development will remain forbidding. Why would any pharmaceutical company risk its assets on the development of an innovative drug?"); Judith L. Wagner, *Should the Pharmaceutical Industry Be a Regulated Utility?* 24(1) HEALTH AFF. 289, 290 (2005) (reviewing MARCIA ANGELL, THE TRUTH ABOUT THE DRUG COMPANIES: HOW THEY DECEIVE US AND WHAT TO DO ABOUT IT (2004)) ("government could curb wasteful and misleading marketing and set reasonable and uniform prices on drugs without endangering the flow of R&D dollars. She argues that marketing dollars would be redirected to R&D. Here again, Angell misunderstands or ignores economics. Investors will not allow funds to be redirected to R&D unless the returns are high enough to justify the risk.")

[481] Marcia Angell, Comment, *The Pharmaceutical Industry – to whom is it accountable?*, 342 (25) NEW ENG. J. MED. 1902, 1904 (2000)

By seeking to impose limits on the extent of permissible profits, such that drug originator firms earn an amount commensurate with their investment and are incentivised to spend more time and effort on drugs with higher health impact, as opposed to ever-greened varieties of existing drugs., the investment protection regime advocated in this thesis comports well with the above framework, where there is increasing pressure to subject pharmaceutical firms to higher levels of regulation.

## CH. V: A TRIPS COMPATIBILITY EVALUATION

### A. Introduction to Article 39.3

This Chapter argues that the investment protection regime as outlined in the last Chapter is compliant with TRIPS, and in particular with Article 39.3 which deals with data protection.

Article 39.3 reads as below:

> Members, when requiring, as a condition of approving the marketing of pharmaceutical or of agricultural chemical products which utilize new chemical entities, the submission of undisclosed test or other data, the origination of which involves a considerable effort, shall protect such data against unfair commercial use. In addition, Members shall protect such data against disclosure, except where necessary to protect the public, or unless steps are taken to ensure that the data are protected against unfair commercial use.

The ambit of Article 39.3[482] hinges significantly on the meaning of the term "unfair commercial use." Currently, there are two main streams of thought. Some TRIPS members such as the U.S. and EU and several industry associations[483] argue that this term translates to an obligation of 'data exclusivity'.[484]

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[482] *See* arts. 39.1 and 39.2 of TRIPS dealing generally with trade secrets, while art. 39.3 deals specifically with regulatory data.

[483] These include the IFPMA (International Federation of Pharmaceutical Manufacturers Association) and EFPIA (European Federation of Pharmaceutical Industries and Associations).

[484] *See* Office of the General Council, U.S. Trade Representative (1995) *as cited in* G. Lee Skillington & Eric M. Solovoy, *The Protection of Test and Other Data Required by Article 39.3 of the TRIPS Agreement*, 24 (1) NW. J. INT'L. L. & BUS. 1 (2003); *see also* EUROPEAN COMMISSION, TBR PROCEEDINGS

As noted in Chapter III, a data exclusivity regime is one where data submitted to a regulatory authority in order to obtain marketing authorization for a new pharmaceutical or agro-chemical compound is prevented from being used by or relied upon by any third party, including a national regulatory authority, for a limited period (normally 5—10 years) from the date of obtaining marketing approval by the originator. By implication, generic producers would have to postpone the launch of their product until the end of this exclusivity period. Alternatively, they could submit their own data, which would oblige them to repeat the clinical trials and generate data afresh.

After the advent of the TRIPS agreement, the Office of the U.S. Trade Representative (hereinafter "USTR") interpreted Article 39.3 of the TRIPS Agreement to mean that:

> [T]he data will not be used to support, clear or otherwise review other applications for marketing approval for a set amount of time unless authorised by the original submitter of the data. Any other

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CONCERNING TURKISH PRACTICES AFFECTING TRADE IN PHARMACEUTICAL PRODUCTS REPORT TO THE TRADE BARRIERS REGULATION COMMITTEE 41 (2004), *available at* http://trade.ec.europa.eu/doclib/docs/2004/october/tradoc_119478.doc; *see also* International Federation of Pharmaceutical Manufacturers Association, *Encouragement of New Clinical Drug Development: The Role of Data Exclusivity*, 4-5 (2000) , *available at* http://www.ifpma.org/documents/nr83/dataexclusivity.pdf; *see also* European Federation of Pharmaceutical Industries and Associations, *TRIPS Article 39.3 (Protection of Undisclosed Data) – A Critical Issue for the Continued Development of Safe and Innovative Medicines for Patients*, 3-4 (EFPIA Position Paper, 2000) , *as cited in* Ingo Meitinger, *Implementation of Test Data Protection according to Article 39.3 TRIPS: The Search for a fair interpretation of the term "unfair commercial use"*, 8 (2) J. WORLD INTELL. PROP. 123 (2005).

> definition of this term would be inconsistent with logic and the negotiating history of the provision.[485]

The EU echoes the US position. In a complaint by the European Federation of Pharmaceutical Industries and Associations (hereinafter "EFPIA") against Turkey for a failure to comply with data protection norms, the European Commission found as below:

> In the light of these considerations and despite certain divergence of opinion, the text, context and purpose of Article 39.3 of TRIPS suggest that in order to guarantee that no "unfair commercial use" within the meaning of Article 39.3 shall be made, regulatory authorities should not rely on these data for a reasonable period of time. In other words, providing data exclusivity for a certain period of time is the envisaged way to protect data against unfair use as prescribed by Article 39.3.[486]

Other member states[487] and industry associations such as the European Generics Medicines Association, however, argue that the term "unfair commercial use" does not necessarily bar a national regulatory authority from relying on originator data to approve a competing generic (referred hereinafter for the sake of convenience as

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[485] *See* Office of the General Council, *supra* note 484.

[486] *See* EUROPEAN COMMISSION, *supra* note 484, concerning a complaint lodged by the EFPIA under Article 4 of Council Regulation (EC) no. 3286/94 (the Trade Barriers Regulation – TBR), to seek the removal of a number of alleged obstacles to trade in pharmaceutical products on the market of the Republic of Turkey.

[487] These include the African Group, Barbados, Bolivia, Brazil, Cuba, Dominican Republic, Ecuador, Honduras, India, Indonesia, Jamaica, Pakistan, Paraguay, Philippines, Peru, Sri Lanka, Thailand and Venezuela. WORLD TRADE ORGANISATION TRIPS COUNCIL, TRIPS AND PUBLIC HEALTH (SUBMISSION BY AFRICAN GROUP AND OTHERS) WTO Doc. IP.C/W/296 (Jun. 20, 2001), *available at* http://commerce.nic.in/ip-c-w-296.pdf.

the "reliance" argument).[488] A group paper submitted by a few developing countries to the TRIPS Council opined:

> [T]he protection is to be granted against "unfair commercial use" of confidential data. This means that a third party could be prevented from using the results of the test undertaken by another company as background for an independent submission for marketing approval, if the data had been acquired through dishonest commercial practices. However, Article 39.3 does permit a national competent authority to rely on data in its possession to assess a second and further applications, relating to the same drug, since this would not imply any "unfair commercial use."[489]

I argue that Article 39.3 does not mandate data exclusivity as a minimal requirement. If it did so, the compensatory liability model outlined in the last Chapter would contravene TRIPS. Prior to a specific assessment of the term "unfair commercial use" to determine its import, it is important to lay out the framework for interpreting WTO provisions.

### B. Interpretative Framework

As per the Understanding On Rules And Procedures Governing The Settlement Of Disputes (Dispute Settlement Understanding or DSU),[490] the

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[488] *See* European Generic Manufacturers Association, *Data Exclusivity: A Major Obstacle to Innovation and Competition in the EU Pharmaceutical Sector* (EGA Position Paper, 2000), 8, *available at* http://www.egagenerics.com/doc/ega_dataex-2000-12.pdf

[489] *See* WORLD TRADE ORGANISATION TRIPS COUNCIL, *supra* note 487, at 9.

[490] Understanding on Rules and Procedures Governing the Settlement of Disputes art. 1, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 2, 1869 U.N.T.S. 401 [hereinafter DSU]. Art. 3.2 of the DSU reads:

Appellate Body is to interpret the provisions of General Agreement on Tariffs and Trade (GATT), 1994 and the other "covered agreements" of the WTO Agreement such as TRIPS 'in accordance with customary rules of interpretation of public international law.' Following this mandate, in *United States - Standards for Reformulated and Conventional Gasoline*,[491] the Appellate Body stressed the need to refer to the fundamental rule of treaty interpretation set out in Article 31(1) of the *Vienna Convention on the Law of Treaties* (hereinafter "Vienna Convention").[492] They held that Article 31(1) and Article 32 of the Vienna Convention 'had attained the status of a rule of customary or general international law.'[493]

Article 31(1) of the Vienna Convention provides that '[a] treaty shall be interpreted in good faith in accordance with the ordinary meaning to be given to the terms of the treaty in their context and in the light of its object and purpose.' Therefore, primary regard is to be given to the ordinary meaning of treaty terms, in context, and in the light of the object and purpose of TRIPS. In the case of ambiguity, Article 32 stipulates that resort may be had to specified supplementary

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> The dispute settlement system of the WTO is a central element in providing security and predictability to the multilateral trading system. The Members recognize that it serves to preserve the rights and obligations of Members under the covered agreements, and to clarify the existing provisions of those agreements in accordance with customary rules of interpretation of public international law. Recommendations and rulings of the DSB cannot add to or diminish the rights and obligations provided in the covered agreements.

[491] *See* Appellate Body Report, *United States- Standards for Reformulated and Conventional Gasoline*, 17, WT/DS2/AB/R (Apr. 29, 1996) [hereinafter US- Gasoline Appellate Body Report].

[492] *See* Vienna Convention on the Law of Treaties, May 23, 1969, 1155 U.N.T.S. 331.

[493] *See* US- Gasoline Appellate Body Report,. *See also* Appellate Body Report, *Japan-Taxes on Alcoholic Beverages*, 9, WT/DS8/AB/R (Nov. 1, 1996) [hereinafter Japan Alcohol Appellate Body Report].

means of interpretation including the "preparatory work of the treaty and the circumstances of its conclusion." [494] In addition, factors such as "subsequent state practice" [495] may be relied upon.

The Appellate Body made clear in its first report that the direction given by Article 3.2 of the Dispute Settlement Understanding (DSU)[496] 'reflects a measure of recognition that the General Agreement is not to be read in clinical isolation from public international law.' [497] In this regard, it bears noting that, of late, the opinions of jurists are gaining recognition and being cited increasingly in Appellate Body and Panel Reports.[498]

[494] *See* art. 32, Vienna Convention on the Law of Treaties, May 23, 1969, 1155 U.N.T.S. 331.

[495] *Id.* Art. 31.3(b)

[496] *See* US-Gasoline Appellate Body Report.

[497] *See* US-Gasoline Appellate Body Report, at 15.

[498] *See* Appellate Body Report, *India-Patent Protection for Pharmaceutical and Agricultural Chemical Products*, WT/DS50/AB/R (Dec. 19, 1997) [hereinafter India Mailbox Appellate Body Report], where the writings of jurists are referred to in footnotes 26, 28 and 52; *see also* MATSUSHITA ET AL., THE WORLD TRADE ORGANISATION: LAW, PRACTICE AND POLICY 66 (3rd ed. 2003) stating that: "The authors of WTO reports… seem to be far more willing than their GATT predecessors to refer to the teachings of highly qualified publicists in justifying their positions."; *see also* Michael Blakeney, *International Intellectual Property Jurisprudence after TRIPS* in INTELLECTUAL PROPERTY IN THE NEW MILLENNIUM 6 (David Vaver & Lionel Bentley eds. 2004) ("In the rapidly developing field of international intellectual property law, the writings of jurists can play an important role in promoting consistency and coherence.").

Despite this elaborate interpretative framework, the WTO panel/appellate body tends towards a predominantly textual approach.[499] In the words of a commentator:

> The Appellate Body has resisted consideration of context, and object and purpose, instead attaching the greatest weight to 'the ordinary meaning to be given to the terms' of the treaty. … The preparatory work of the treaty has been accorded even less weight, because of the secondary rank attributed to this criterion by the Vienna Convention, the lack of reliable records, and the ambiguities resulting from the presence of contradictory statements of the negotiating parties.[500]

As to the weight to be accorded to panel/appellate body decisions, the Appellate Body in Japan Alcohol Appellate Body Report noted that although they were not

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[499] *See* Graeme B. Dinwoodie & Rochelle Cooper Dreyfuss, *WTO Dispute Resolution and the Preservation of the Public Domain of Science under International Law*, *in* INTERNATIONAL PUBLIC GOODS AND TRANSFER OF TECHNOLOGY UNDER A GLOBALIZED INTELLECTUAL PROPERTY REGIME 866 (Keith E. Maskus & J. H. Reichman eds., 2005) ("[W]e inform our analysis with the observation that WTO panels tend to hew closely to text when resolving disputes."); *see also* William Magnuson, *WTO Jurisprudence & Its Critiques: The Appellate Body's Anti-Constitutional Resistance*, 51 HARV. INT'L. L. J. 121, 125 (2010) ("[A]ll sides agree that the AB has clearly adopted narrow textualism as its presiding methodology of treaty interpretation.").

[500] *See* Richard Steinberg, *Judicial Lawmaking at the WTO: Discursive, Constitutional, and Political Constraints*, 98 AM. J. INT'L. L. 247, 261 (2004) ("According to Claus-Dieter Ehlermann, a former member of the Appellate Body, this bias was adopted to protect the Appellate Body from 'criticism that its reports have added to or diminished the rights and obligations provided in the covered agreements,' which would contravene DSU Article 3.2."); *see also* Jerome H. Reichman, *The TRIPS Agreement Comes of Age: Conflict or Cooperation with the Developing Countries?* 32 CASE W. RES. J. INT'L. L. 441, 446 (2000) (stating in relation to the India Mailbox Appellate Body Report:"In its ground-breaking opinion, the Appellate Body opted for a strict constructionist interpretation of the TRIPS Agreement, in keeping with its view of Article 31 of the Vienna Convention on the Law of Treaties."); *see generally* Petros C. Mavroidis, *No Outsourcing of Law? WTO Law as Practiced by WTO Courts*, 102 AM. J. INT'L. L. 421, 456 (2008) (noting that WTO adjudicating bodies have first tried to exhaust the references of Article 31 of the Vienna Convention before moving to Article 32 in an overwhelming number of cases, thereby indicating its supplementary nature).

binding, they "create legitimate expectations among WTO Members, and therefore, should be taken into account where they are relevant to any dispute."[501]

However, a commentator rightly notes that, "in general, previous decisions and doctrine are so highly persuasive in WTO jurisprudence, and their use is so central to the discourse of dispute settlement, that it may be said that the WTO observes de facto *stare decisis*."[502]

Using the above framework, I argue that a compensatory liability model is compatible with Article 39.3 of TRIPS.

### C. Article 39.3 and Data Exclusivity

The ordinary meaning of the terms used in Article 39.3, construed in the context of the term "unfair competition" in the Paris Convention, and more importantly, the negotiating history of Article 39.3, cast doubt on the view that Article 39.3 mandates data exclusivity.[503]

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[501] *See* Japan Alcohol Appellate Body Report, at 13. The Appellate Body explained:

> Adopted panel reports are an important part of the GATT acquis. They are often considered by subsequent panels. They create legitimate expectations among WTO Members, and therefore, should be taken into account where they are relevant to any dispute. However, they are not binding, except with respect to resolving the particular dispute between the parties to that dispute.

[502] *See* Steinberg, *supra* note 500, at 7; *see also* Noemi Gal-Or, *The Concept of Appeal in International Dispute Settlement*, 19(1) EUR. J. INT'L. L. 43, 53-4 (2008).

[503] *See* Panel Report, *Argentina -Patent Protection for Pharmaceuticals and Test Data Protection for Agricultural Chemicals*, WT/DS171/3,WT/DS196/4 (Jun. 20, 2002) (An excellent opportunity for a

As noted earlier, the Vienna Convention on the law of treaties[504] is the main interpretative tool used in WTO jurisprudence today. Article 31.1 of the Vienna Convention states that, "a treaty shall be interpreted in good faith in accordance with the ordinary meaning to be given to the terms of the treaty in their context and in the light of its object and purpose."

For the sake of convenience, I deal first with an interpretation of the term 'unfair' before moving on to "commercial" and "use." Determining the ordinary meaning of a term is always the first step in treaty interpretation and a dictionary is a good reference point in this regard.[505] The Concise Oxford Dictionary (1989) defines "unfair" as "not equitable or honest or impartial or according to rules." However, since the meanings of 'inequitable' or "dishonest" are no less disputable than that of "unfair," the dictionary meaning does not get us very far.[506] Let us, therefore, look to other factors such as the "context" in which this term is used. One such "context" is supplied by the Paris Convention.[507] Article 39.1 states:

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panel ruling in this regard was lost when the US withdrew its complaint against Argentina alleging that in not providing for data exclusivity, Argentine law contravened Article 39.3. On 20 June 2002, the USA and Argentina notified the DSB of a mutually agreed solution.).

[504] *See* Vienna Convention on the Law of Treaties, May 23, 1969, 1155 U.N.T.S. 331.

[505]*See* Dinwoodie and Dreyfuss, *supra* note 499, at 1005-6 ("Webster's has become an essential research tool in WTO TRIPS litigation.").

[506]*See* Fellmeth, *supra* note 42, at 461; *see also* Appellate Body Report, *Canada-Measures Affecting the Export of Civilian Aircraft*, 153, WT/DS70/AB/R (Aug. 2, 1999) ("[D]ictionary meanings leave many interpretive questions open.").

[507] *See* Paris Convention for The Protection of Industrial Property, Mar. 20, 1883, 21 U.S.T. 1583, 828 U.N.T.S. 305 [hereinafter Paris Convention].

> In the course of ensuring effective protection against unfair competition as provided in Article 10bis of the Paris Convention (1967), Members shall protect undisclosed information in accordance with paragraph 2 and data submitted to governments or governmental agencies in accordance with paragraph 3.

Article 39.3 is, therefore, based on and develops the disciplines on unfair competition contained in Article 10*bis* of the Paris Convention, for the particular case of regulatory information. Hence, the interpretation of the Convention is of relevance to the interpretation of Article 39.3.[508] The first two clauses of Article 10*bis* of the Paris Convention read as below:

> (1) The countries of the Union are bound to assure to nationals of such countries effective protection against unfair competition.
> (2) Any act of competition contrary to honest practices in industrial or commercial matters constitutes an act of unfair competition.

Bodenhausen notes that not only is the term "unfair" flexible, but as to what constitutes "competition" is to be determined in each country according to its concepts.[509] Ladas observes:

> Morality, which is the source of the law of unfair competition, is a simple notion in theory only. In fact it reflects customs and habits anchored in the spirit of a particular community. There is no clearly objective standard of feeling, instincts, or attitudes toward a certain

[508] *See* UNCTAD-ICTSD, RESOURCE BOOK ON TRIPS AND DEVELOPMENT: AN AUTHORITATIVE AND PRACTICAL GUIDE TO THE TRIPS AGREEMENT 533 (2004).

[509] *See* G.H.C. BODENHAUSEN, GUIDE TO THE APPLICATION OF THE PARIS CONVENTION FOR THE PROTECTION OF INDUSTRIAL PROPERTY 144 (1968).

> conduct. Therefore, specific prescriptions involving uniform evaluation of certain acts are extremely difficult.[510]

In short, concepts such as "unfair" or "honest" are relative to the values of a particular society at a given point in time. It varies among Members, and this variation is one of the premises on which the discipline of unfair competition is grounded.[511] A study of the Paris Convention and the literature on its interpretation leaves us in the same position from where we started i.e. the term "unfair" is relative, and there is no universal understanding of the same. It is, therefore, important to look to other factors such as the negotiating history of TRIPS.

Article 32 of the Vienna Convention stipulates that when the ordinary meaning of a term is ambiguous, resort may be had to specified supplementary means of interpretation including the "preparatory work of the treaty and the circumstances of its conclusion." The drafting history of the TRIPS Agreement reveals that an earlier draft at the Brussels Ministerial Meeting 1990 (hereinafter "Brussels Draft") included a "data exclusivity" clause.[512] Article 4A of the Brussels Draft reads as below:

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[510] *See* S. LADAS, PATENTS, TRADEMARKS AND RELATED RIGHTS – NATIONAL AND INTERNATIONAL PROTECTION 1685 (1975).

[511]*See* Carlos Correa, *Protection of Data Submitted for the Registration of Pharmaceuticals: Implementing the Standards of the TRIPS Agreement*, 25 (South Centre, 2002), *available at* http://apps.who.int/medicinedocs/pdf/h3009ae/h3009ae.pdf.

[512] *See* GATT Secretariat, *Draft Final Act Embodying the Results of the Uruguay Round of Multilateral Trade Negotiations,* MTN.TNC/W/35 Rev.1 (Nov. 26, 1990), *as cited in* DANIEL GERVAIS, THE TRIPS AGREEMENT, DRAFTING HISTORY AND ANALYSIS 182 (2003).

> Parties, when requiring, as a condition of approving the marketing of new pharmaceutical product or of a new agricultural chemical product, the submission of undisclosed test or other data, the originator of which involves a considerable effort shall [protect such data against unfair commercial use. Unless the person submitting the information agrees, the data may not be relied upon for the approval of competing products for a reasonable time**,** generally no less than five years, commensurate with the efforts involved in the organization of the data, their nature and the expenditure involved in their preparation. In addition, parties shall] protect such data against disclosure, except where necessary to protect the public.[513]

But this was removed in the final TRIPS text. The fact that a clause from an earlier draft mandating data exclusivity was not included in the final text could be taken to signal the intent of the international community in preferring a more flexible approach than a categorical 'data exclusivity' mandate under TRIPS.**[514]**

Reichman argues that any interpretation in favour of data exclusivity would violate the teachings of the India Mailbox Appellate Body Report,[515] where the Appellate Body stressed the importance of both Article 19 of the Understanding on the Settlement of Disputes (DSU) and Article 1.1 of the TRIPS Agreement.[516] The

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[513] *See* Jerome H. Reichman, *Undisclosed Clinical Trial Data under the TRIPS Agreement and its Progeny: A Broader Perspective* (UNCTAD-ICTSD, 2004), 9, *available at* http://www.iprsonline.org/unctadictsd/bellagio/docs/Reichman_Bellagio4.pdf (The bracketed provision marks off the US and EU positions from that of other countries opposed to this new form of protection for regulatory data).

[514] To ignore the clear evolution of the text in favour of quasi-exclusive rights in regulatory data, in a form that was proposed but ultimately excised from the Final Act, would in effect amount to imposing unbargained-for trade concessions under a discredited "TRIPS plus approach" that has no legal foundation whatsoever.

*Id.* at 10.

[515] *See* India Mailbox Appellate Body Report.

[516] *See* Reichman, *supra* note 513, at 13.

former provides that a WTO Panel "cannot add to or subtract from the covered obligations," while the latter provision states that "members shall be free to determine the appropriate method of implementing the provisions of this Agreement within their own legal system and practice."

Having said this, it is important to emphasise that TRIPS is only a "minimum standards" legislation and any member state is free to include a data exclusivity obligation in its national legislation, if its policy imperatives so demand. Although "unfair competition" is categorized as one species of "intellectual property" by TRIPS, it does not automatically translate to an exclusive property right, in the way that a patent does.[517] This view has been adopted by a number of developing countries:

> Article 39.3 of the TRIPS Agreement leaves considerable room for Member countries to implement the obligation to protect test data against unfair competition practices. The Agreement provides that "undisclosed information" is regulated under the discipline of unfair competition, as contained in article 10 bis of the Paris Convention. With this provision, the Agreement clearly avoids the treatment of undisclosed information as a "property" and does not require granting "exclusive" rights to the owner of the data.[518]

The United Nations Conference on Trade and Development [UNCTAD][519] and the World Health Organization (WHO) Intellectual Property Commission (2006)[520]

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[517] *See* UNCTAD-ICTSD, *supra* note 508, at 527. (*"*Such protection requires, as mentioned, remedial action against 'dishonest' commercial practices, but does not give rise to exclusive rights.").

[518] *See* WORLD TRADE ORGANISATION TRIPS COUNCIL, *supra* note 487.

[519] *See* UNCTAD-ICTSD, *supra* note 508, at 526.

have adopted similar interpretations of Article 39.3 as well. It is interesting to note that the World Intellectual Property Organisation (WIPO), an organisation that is heavily criticised for unduly favouring increased intellectual property protection at the expense of LDC's and developing countries,[521] published a model law containing a provision worded similarly to Article 39.3 of TRIPS Agreement:

> Any act or practice, in the course of industrial or commercial activities, shall be considered an act of unfair competition if it consists or results in an unfair commercial use of secret test or other data, the origination of which have been submitted to a competent authority for the purposes of obtaining approval of the marketing of pharmaceutical or agricultural chemical products which utilize new chemical entities.[522]

Contrast this with the North American Free Trade Agreement (NAFTA), which introduced explicit provisions on data exclusivity, even prior to the coming into force of TRIPS:

> Each Party shall provide that for data subject to paragraph 5 that are submitted to the Party after the date of entry into force of this Agreement, no person other than the person that submitted them may, without the latter's permission, rely on such data in support of

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[520] *See* WORLD HEALTH ORGANIZATION, INNOVATION AND PUBLIC HEALTH: REPORT OF THE COMMISSION ON INTELLECTUAL PROPERTY RIGHTS, INNOVATION AND PUBLIC HEALTH 143 (2006), *available at* http://www.who.int/intellectualproperty/documents/thereport/ENPublicHealthReport.pdf

[521] WIPO is currently engaged in norm-setting activities in various technical Committees. Some of these activities would have developing countries and LDCs agree to IP protection standards that largely exceed existing obligations under the WTO's TRIPS Agreement, while these countries are still struggling with the costly process of implementing TRIPS itself. WIPO, *Proposal By Argentina And Brazil For The Establishment Of A Development Agenda For WIPO* WO/GA/31/11 (27 August, 2004), *available at* http://www.wipo.int/documents/en/document/govbody/wo_gb_ga/pdf/wo_ga_31_11.pdf.

[522] *See* art. 6(4), *WIPO Model Provisions on Protection Against Unfair Competition* (1996). (This model law was published after the coming into force of the TRIPS Agreement.).

> an application for the product approval during a reasonable period of time after their submission…[523]

This suggests that the TRIPS wordings are more flexible on this count and cannot be read to mandate data exclusivity.[524] The interpretative principle of *in dubio mitius* applies and one cannot "lightly assume that sovereign states intended to impose upon themselves the more onerous, rather than the less burdensome, obligation…."[525] Rather, since the meaning of the term "unfair commercial use" is ambiguous, "that meaning is to be preferred which is less onerous to the party assuming an obligation, or which interferes less with the territorial and personal supremacy of a party, or involves less general restrictions upon the parties."[526]

To conclude, an appreciation of the relativity of the term "unfair," coupled with the text of Article 39.3 and the negotiation history suggest that Article 39.3 does not mandate an exclusive property right, as its minimal requirement.

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[523] *See* North American Free Trade Agreement, U.S.-Can.-Mex., art. 1711, ¶6, Dec. 17, 1992, 32 I.L.M. 605 [hereinafter NAFTA].

[524] *See* JAYASHREE WATAL, INTELLECTUAL PROPERTY RIGHTS IN THE WTO AND DEVELOPING COUNTRIES 204 (2001).

[525] *See* Appellate Body Report, *European Communities - Measures Concerning Meat and Meat Products (Hormones),* ¶ 165, WT/DS48/AB/R, WT/DS26/AB/R (Jan. 16, 1998).

[526] *See id.*

A potential argument in favour of data exclusivity might be based on "state practice."[527] However, member states have adopted differing approaches to protecting regulatory data—while the U.S., EU, Australia, New Zealand and Israel provide for data exclusivity, countries such as Russia, Turkey and South Africa do not currently do so.[528] Therefore, there is no evidence of "a concordant, common and consistent sequence of acts or pronouncements which is sufficient to establish a discernible pattern implying the agreement of the parties [to a treaty] regarding its interpretation…"[529] Further, even those member states that have adopted data exclusivity in their domestic laws,[530] have done so without acknowledging that such a duty exists under Article 39.3.[531]

### D. The Appropriate Standard of Protection?

The above discussion makes clear that data exclusivity is not the minimum mandatory standard under Article 39.3. What then is the standard? Owing to the

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[527] *See* art. 31.3(b), which expands on art. 31.1 by stating that while interpreting a treaty term, in addition to the context, one has to also take into account "any subsequent practice in the application of the treaty which establishes the agreement of the parties regarding its interpretation."

[528] *See* International Federation of Pharmaceutical Manufacturers Association, *supra* note 237..

[529] *See* Japan Alcohol Appellate Body Report, at 13.

[530] Some of them have done so under bilateral free trade agreements (FTAs) signed with the US. Chile is a good example, with the US Chile FTA containing an express provision on data exclusivity for a period of 5 years. Free Trade Agreement, U.S.-Chile, art. 17.10.1, 6 June, 2003, 42 I.L.M. 1026 (entered into force on Jan. 1, 2004); *see also* Pedro Roffe, *Bilateral Agreements and a TRIPS Plus World*, 24 (Quaker Affairs International Programme, Issues Paper No. 4, 2004), *available at* http://www.twnside.org.sg/title2/FTAs/Intellectual_Property/IP_and_other_Topics/Chile-USAFTAP.Roffe.pdf (analysing the US Chile FTA discussed above); *see also* Fellmeth, *supra* note 42, at 455 (noting that other countries such as Sri Lanka, Laos, Cambodia, Vietnam and Singapore have signed similar bilateral FTA's with the US).

[531] *See* Fellmeth, *supra* note 42, at 455.

tortuous wording and rather ambiguous legislative history, it is difficult to pin down the appropriate standard for protecting data under Article 39.3. Some countries and scholars argue that a mere legal obligation to protect the data from fraudulent disclosure would comply with Article 39.3. They argue that Article 39.3 does not bar the reliance by a regulatory authority on originator data for the purpose of approving a competing generic product i.e. the "reliance" argument already referred to earlier. Such an interpretation is based on the definitional flexibility that inheres in the word "unfair." Correa notes:

> Many countries do not treat commercialization of a "similar" product approved by reference to a previous registration, or by reliance on data submitted by the originator company, as an unfair commercial practice, but some do. Under Article 39.3, each approach is valid. Article 39.3 mandates protection against "unfair commercial practices", but permits Member countries to determine which practices will be deemed commercially unfair.[532]

In a recent piece, Christopher Wadlow endorses the "reliance" argument by arguing that member states do not commit acts of "unfair" competition by referring to the filed data of the original applicant in evaluating subsequent applications for marketing approval.[533] He bases this flexibility on the term "unfair" and the jurisprudence developed under Article 10*bis* of the Paris Convention in this regard.[534]

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[532] *See* Correa, *supra* note 511, at 28

[533] *See* Christopher Wadlow, *Regulatory Data Protection under TRIPS Article 39(3) and Article 10bis of the Paris Convention: Is there a Doctor in the House?*, 4 INTELL. PROP. Q. 355, 389 (2008).

[534] *See id.* at 367.

I have, in the past, contested the TRIPS compatibility of the "reliance" argument on the ground that it results in rendering Article 39.3 redundant.[535] If reliance were permitted under Article 39.3, it would mean that only acts of deliberate leakage and fraud of trial data remained within the ambit of Article 39.3. Such acts of deliberate fraud or disclosure could well be subsumed under the broad rubric of Article 39.1, rendering the core essence of Article 39.3 redundant.

In this thesis however, I do not aim to delve into that debate to evaluate the minimum standard of compliance mandated under Article 39.3 and to conclusively establish whether or not a "reliance" regime is likely to comply with TRIPS. Rather, my limited focus is to assess whether a compensatory liability regime, whereby the data originator does not have exclusivity over the market, but only a right to be remunerated adequately by subsequent market entrants, complies with the TRIPS mandate to protect data. This would essentially turn upon whether or not the above mentioned remuneration is a "fair" one under Article 39.3? If so, then the use of the data does not amount to an "unfair commercial use." The EU hints at the possibility that this sort of an intermediate standard may be compatible with Article 39.3:

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[535] *See* Shamnad Basheer, *Protection of Regulatory Data Under Article 39.3 of TRIPS: The Indian Context*, (Intellectual Property Institute, 2006), http://papers.ssrn.com/sol3/papers.cfm?abstract_id=934269.

> In theory, Article 39.3 appears to give Members the discretion to provide for different means of data protection, although it is very difficult to imagine other ways than non-reliance over a certain period of time, except for a (temporary) refusal to grant any second market approval to similar products (even if the second applicant submits its own data), as is the case in at least one WTO Member and maybe for an obligation to pay as a compensation for reliance on proprietary data without having to obtain consent from the first applicant.[536]

Needless to state, in the context of the fact that the EU has maintained that Article 39.3 calls for nothing less than data exclusivity, the above statement appears a *volte-face* in the EU position. Perhaps this explains why the possibility of a compensation scheme being treated as compatible with Article 39.3 is not expressed as clearly and strongly as it ought to be by the EU, but rather prefixed with an 'and maybe for an obligation….'. The EU also goes to doubt the practicality of such a compensatory scheme.[537]

Scholars also point to the possibility of Article 39.3 envisaging a 'compensatory liability' standard.[538] In particular, Fellmeth notes:

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[536] *See* European Union, *Questions on TRIPS and Data Exclusivity: An EU Contribution*, 20 (2001), *available at* http://trade.ec.europa.eu/doclib/docs/2006/may/tradoc_122031.pdf

[537] > The question remains whether such payment would indeed be sufficient to guarantee that any "unfair commercial use" of test data takes place. For instance, it would be essential that such payment reflects the investments made by the original applicant -- which may not always be easy to establish. In theory, any country maintaining an effective system to implement obligations under 39.3 even if different from non-reliance over time, would not be in breach of its TRIPS obligations, but we are not aware of many alternatives and it is clear that what the TRIPS-negotiations had in mind was data exclusivity over a certain period of time.

*Id.* at 17.

[538] *See* Fellmeth, *supra* note 42; *see also* Meitinger, *supra* note 484, at 134-5.

> Obviously, a blanket refusal by a drug regulatory authority to disclose or to allow reliance on the trade secret would prevent unfair commercial use. But there are other means for protecting against unfair use that do not require providing a monopoly on the marketing approval data. The purpose of the duties of confidentiality and of data exclusivity may be satisfied even when the data has been released to a competitor of the initial registrant, or a competitor has been permitted to rely on the data, or both. In these instances, the drug regulatory authority must ensure that adequate compensation renders the disclosure and use of the data economically "fair".[539]

In short, a compensatory liability model where the data can be relied upon, only when some "fair" compensation is provided to the originator of the data is likely to be TRIPS compliant.[540] Such a "compensatory liability" model is different from a "data exclusivity" regime, where the originator is guaranteed complete market exclusivity and can prevent any use of the data by a competitor. In a "compensatory liability" model, however, there is no exclusivity and data can be used in favour of competitors, upon the payment of a "fair" compensation.

## E. Time Frame for Protection under Article 39.3

[539] *See* Fellmeth, *supra* note 42.

[540] This term 'compensatory liability' has been used by scholars such as Reichman, *supra* note 513, at 14 and Dinca, *supra* note 431, at 549.

Article 39.3 throws up another unresolved issue: Unlike Article 28 of TRIPS which mandates patent protection for a minimum period of 20 years, Article 39.3 does not call for any specific period of protection. Member states are, therefore, free to determine the appropriate time frame in their respective local legislations, with the caveat that any such time frame must be "fair" (i.e. targeted to prevent the unfair use of regulatory data) and not with a view to rendering the obligation redundant.

As noted earlier in this paper, a prior Brussels Draft (1990) had provided that data exclusivity had to run "for a reasonable time, generally no less than five years." The exclusion of this clause from the final version of TRIPS would mean that member states have flexibility to determine a time frame in accordance with their national interest. As with the differences in the extent of protection provided by member states to regulatory data, the time periods of protection also vary. Illustratively, the U.S. provides for a general data exclusivity period of 5 years to new drug registrants,[541] while the EU provides for a longer period of protection captured by the "8+2+1" formula.[542] One cannot, therefore, discern a "concordant, common and consistent" sequence of acts or pronouncements in favour of the 5 year data exclusivity period, as would be sufficient to constitute 'state practice'

[541] *See* Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified in Titles 15, 21, 28, and 35 of the U.S. Code). (This Act now provides "five years [of] such protection for new chemical entities and three years for data filed in support of... chemical entities which have already been approved for use in medicines but [for] which fresh authorizations are [to be] based on new clinical investigations."); *see also* COOK, *supra* note 278, at 401.

[542] *See* discussion in Chapter III: Data Exclusivity and Pharmaceutical Innovation, *supra* text accompanying notes 260-261.

under Article 31.3 of the Vienna Convention.

Based on the above discussion, it is clear that a compensatory liability model which operates for a period of time until such time as the originator recovers her costs along with an appropriate rate of return on investment is likely to comply with Article 39.3 of TRIPS.

## CH. VI: PATENTS, UPSTREAM INVENTIONS AND INCENTIVES

My central argument in this thesis is that an investment protection regime is far more optimal than either a patent regime or a data exclusivity regime in fostering higher levels of investment into drug discovery and development. I, therefore, propose that countries discard their existing data exclusivity regimes.

However, what of the patent regime? Can countries dispense with this as well, in the specific context of pharmaceutical innovation? Chapter II explored the various theories underlying patent protection and found that none of them offer any persuasive support for the patent system. In particular, the incentive theory is yet to find strong empirical support. Notwithstanding this lack of persuasive theory or evidence favouring the patent system, I argue that countries ought not to dispense with the patent system altogether.

Firstly, owing to the binding nature of TRIPS, countries do not have the luxury of doing away with the patent system altogether. Rather, they have to mandatorily provide a 20 year patent protection for all "inventions" that are new, useful and inventive.[543]

Secondly, although there is no conclusive evidence pointing to the role of

[543] *See* TRIPS, art. 27 (mandating that patents be granted to all inventions that are new, inventive and useful).

patents in accelerating innovation, there is no evidence pointing the other way as well. This inconclusiveness led eminent economist Penrose to note several decades ago that:

> If national patent laws did not exist, it would be difficult to make a conclusive case for introducing them; but the fact that they do exist, shifts the burden of proof and it is equally difficult to make a really conclusive case for abolishing them.[544]

In a similar vein, Fritz Machlup concluded:

> If we did not have a patent system, it would be irresponsible, on the basis of our present knowledge of its economic consequences, to recommend instituting one. But since we have had a patent system for a long time, it would be irresponsible, on the basis of our present knowledge, to recommend abolishing it.[545]

The situation is not vastly different today.[546]

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[544] *See* EDITH PENROSE, THE ECONOMICS OF THE INTERNATIONAL PATENT SYSTEM (1951). Bronwyn Hall comments on this remark by Penrose as follows: "One possible interpretation of this remark is that history matters, in the sense that industrial organizations and firms adapt to the institutional regime in which they operate and changing this regime, whatever it is, involves substantial short-term costs that may not be outweighed by the long-term benefits." For further discussion, see Hall, *supra* note 3, at 575.

[545] *See* MACHLUP, *supra* note 211.Machlup further states that. "No economist, on the basis of present knowledge, could possibly state with certainty that the patent system, as it now operates, confers a net benefit or net loss upon society."

[546] S*ee* Paul Belleflamme, *Patents and Incentives to Innovate: Some Theoretical and Empirical Economic Evidence*, 13(2) J. EURO. ETHICS NETWORK 267, 284 (2006) (noting that, "[E]ven though a completely new body of empirical and theoretical knowledge has emerged since then, we are still unable to revise Penrose's and Machlup's views."). He further states:

> We are, however, able to refine the evaluation, as recent economic analysis has brought to light previously unsuspected costs and benefits of the patent system. Among these costs are the ones linked to the administration of the system. So rather than questioning the *raison d'etre* of patents, today's economists propose ways of correcting their shortcomings.

Owing to the above reasons, I suggest a cautious approach to patents and note that in the absence of more compelling evidence, countries ought not to dispense with the patent system altogether. The retention of the patent system could also offer some additional incentives to upstream third party inventors i.e. entities that are different from drug originators, and whose upstream inventions are used by drug originators to arrive at the final drug. This is discussed in detail below.

### A. Upstream Inventions and Incentives

This thesis has proceeded on the assumption that the drug originator is singularly responsible for the discovery and development of a drug. However, the current pharmaceutical innovation framework is such that the discoverer of the drug molecule[547] may not necessarily be the same as the entity that finally develops and markets the drug.[548] This is particularly true for biologics.[549]

[547] Drug discovery refers to all steps commencing immediately after the identification of a disease target and includes the identification of an appropriate lead to inhibit the target and the filing of an IND covering that particular target. Discussion in Chapter I *supra* text accompanying notes 25-30.

[548] Drug Development is defined in this thesis as covering all stages that commence immediately after the procurement of IND approval and covers all human clinical trials and all other steps that are required to obtain final drug regulatory approval. Discussion in Chapter I, *supra* text accompanying notes 31-40.

[549] *See* Morgan, *supra* note 256, at 117.

There is considerable debate surrounding the number of new drugs that are based on upstream inventions attributable to third parties.[550] A recent study indicates that approximately half of all drugs that were granted priority review (indicating thereby, that they catered to unmet medical needs) and approved by the U.S. FDA during 1998-2007 emanated from small biotechnology firms or universities.[551]

This trend is likely to accelerate in future and any model for incentivising drug discovery and development ought to factor in this possibility, of upstream inventions being attributable to a party other than the final drug originator.[552] The rate of inventive output from such third parties depends to a large extent on the

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[550] While some studies examine the issue by considering only inventions patented by universities and public funded research institutions. Sampat, *supra* note 19; Other studies take into account upstream discoveries by small biotechnology firms as well. Robert Kneller investigated 123 drugs, being conventional chemical drugs and not biologics, that had been granted priority review and approved by the U.S. FDA from 1998 to 2007 and the patents associated with them. Of these 123 drugs, only 46% of the patents corresponding to whole drug equivalents (WDE) were attributed to the big pharmaceutical companies. Of the remaining 54%, 30% came from small biotech firms and 24% from biotechnology firms. *See* Robert Kneller, *The Importance of New Companies for Drug Discovery: Origins of a decade of New drugs*, 9 NATURE REVIEWS DRUG DISCOVERY 867 (2010).

[551] It is important to note however in many cases, small biotech firms responsible for upstream inventions (or ones that acquired inventions from the discovering universities) filed the new drug application (NDA) application themselves; it is estimated that such NDA filings amounted to 60% (51 out of 86) of total filings considered in the article. The remaining 40% were divided approximately evenly between drugs that were taken through to FDA approval by another biotechnology company or by a pharmaceutical company. It is pertinent to note that the contribution of small biotech firms and universities to the total number of new drugs (and not just the most innovative drugs) approved during this time frame was much lower. Kneller, *supra* note 550.

[552] *See* Bruce Rasmussen, *Response of Pharmaceutical Companies to Biotechnology: Structure and Business Model*, 4 (Centre for Strategic Economic Studies, Working Paper No. 33, 2007) http://www.cfses.com/documents/pharma/33-Pharmaceutical_Business_Models_Rasmussen.pdf ("Prior to the advent of biotechnology, the structure of the value chain of the individual pharmaceutical company was relatively self-contained. Each pharmaceutical company was fully integrated, conducting its own research, development, manufacturing and distribution of its own drugs.").

kind of incentives that exist at these upstream stages.

The section below attempts to draw out the potential incentives that exist for upstream third party research. One might consider the following alternative scenarios pertaining to upstream research:

(i) where the upstream research is conducted by a public funded institution or entity;[553] and

(ii) where the upstream research is conducted by a private firm or entity.

In so far as scenario (i) is concerned, it is reasonable to expect that public funding will continue even in the absence of patents and recoverable license fees.[554] Such funding, in most cases, is not contingent upon whether the money spent on research is recoverable financially through market monopolies and patents. Although the advent of regimes such as the US Bayh-Dole Act[555] may have changed

[553] The global expenditures for health research from public funds are quite significant. It is estimated that direct expenditures from public funds accounted for about 45% of the total amount of healthcare expenditure in 2003 i.e. approximately U.S. $56.1 billion out of a total of U.S. $125.8 billion. *See* Global Forum for Health Research, *Monitoring Financial Flows for Health Research available at* http://announcementsfiles.cohred.org/gfhr_pub/assoc/s14826e/s14826e.pdf. (last visited: May 22, 2012)..

[554] *See* Kevin Outterson, *Should Access to Medicines and TRIPS Flexibilities be Limited to Specific Diseases*, 34 AM. J. L. & MED. 279, 288 (2008) (arguing that after adjustments of tax credits, etc, direct public investments in health R&D are probably significantly larger than private for-profit investments).

[555] *See* University and Small Business Patent Procedures Act, 35 U.S.C. §§ 200-212 (1980).

this equation to some extent,[556] it would be fair to state that public funding is not likely to wither away in the absence of patent protection for inventions ensuing from such funding.

### 1. A New IND Right

Private firms or institutions contributing to the drug discovery process may be reluctant to invest in R&D without some form of legal protection that helps recoup expensive investment.

It bears reiteration that although the most significant component of the expenses associated with drug discovery and development are attributable to clinical trials, the process of drug discovery leading up to the filing of an Investigative New Drug Application (INDA)[557] or an equivalent Clinical Trial Authorisation (CTA) application in the EU[558] also comes with significant expenditure and risk.[559]

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[556] *See* Jennifer Henderson & John Smith, *Academia, Industry and the Bayh-Dole Act: An Implied Duty to Commercialize*, 4-5 (Oct. 2002), http://www.cimit.org/news/regulatory/coi_part3.pdf; *see also* John Raubitschek, *Responsibilities under the Bayh Dole Act*, 87 J. PAT. & TRADEMARK OFF. SOC'Y 311, 313-314 (2005).

[557] As discussed in Chapter I, an INDA is an application seeking permission from the FDA to test a drug candidate in humans. This application contains lab-tested and other preclinical evidence to demonstrate that the drug is sufficiently effective and safe to be tested in humans. Once the INDA is submitted, the sponsor must wait 30 calendar days before initiating any clinical trials. During this time, the FDA has an opportunity to review the INDA. U.S. FDA, *Investigational New Drug Application*, http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm (last visited: Sept. 27, 2011).

[558] The EU follows a similar procedure to the U.S., where prior to the start of human trials, the sponsor must request authorization to conduct clinical trials through a submission called a Clinical

Some upstream entities are likely to possess the technological and the financial wherewithal to take a drug molecule up to the INDA or the CTA stage, but not to the clinical trial stage.[560] I, therefore, propose a separate exclusivity right in favour of such entities, wherein the mere filing of an INDA or CTA triggers a right to claim reimbursement of all costs associated with the drug discovery up to the time of filing of the said INDA or CTA. However, such right is contingent upon the final approval of the drug in question by the regulatory authority. The proposed contingent right is elaborated upon below:

If an IND or CTA applicant does not choose to pursue the INDA and conduct clinical trials, it must make its intentions known to the drug regulator (FDA or EMEA). The IND or the CTA application is then thrown open to any interested third party to pursue, and the said party may apply to the FDA or EMEA to conduct human trials based upon the filed INDA/CTA.

If the said third party firm achieves final drug regulatory approval, it ought to offer due credit to the INDA or CTA applicant. In this way, one might consider

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Trial Authorisation (CTA). This application includes a group of scientific documents called an Investigational Medicinal Products Dossier (IMPD); *see* WOOD, *supra* note 34.

[559] Of the total U.S. $802 million stated to be the average cost associated with drug discovery and development, the costs associated with the drug discovery stage amount to U.S. $335 million. DiMasi, *supra* note 43 and accompanying text.

[560] *See generally* Kneller, *supra* note 550; *see also* Yu-shan Su et al., *How Small Firms can benefit from Open Innovation? – Evidence from Taiwanese Biotechnology Firms*, 4, *available at* http://www2.druid.dk/conferences/viewpaper.php ?id=501961&cf=43 (last visited Sept. 27, 2011).

both the INDA/CTA applicant and the firm that finally obtains regulatory approval to be joint drug originators, with equal entitlement to claim paternity over the drug, in much the same way that some copyright regimes offer moral (paternity) rights to authors.[561] While applying what is predominantly a copyright law concept to a pharmaceutical innovation context, one may require some adaptation. Illustratively, one could simply articulate the specific moral obligation, requiring a drug manufacturer to identify the IND/CTA applicant as a joint drug originator, in any labelling/packaging accompanying the drug.

The existence of a contingent right in favour of the IND/CTA filer also means that any firm, which wishes to take the drug through trials can only do so after entering into a prior agreement with the IND/CTA applicant and such agreement may provide for payments to the IND/CTA filer.[562]

In order for such a contingent pre-clinical trial right to operate in favour of the IND/CTA applicant, it is important that the law also provide that the IND/CTA applicant in respect of a certain drug molecule be provided the exclusive right to

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[561] *See* Mira T. Sundara Rajan, *Moral Rights and Copyright Harmonisation: Prospects for an 'International Moral Right"?* (17th B I LETA Annual Conference, Free University, Amsterdam, April 5-6, 2002) (noting that the copyright regimes of many countries provide for what are commonly labelled as moral rights. The two most widely recognised moral rights are the right of attribution or paternity, ensuring that the author is acknowledged as the creator of her own work, and the right of integrity, which allows an author to protest mistreatment or abuse of her work); *see also* Cyrill P. Rigamonti, *Deconstructing Moral Rights,* 47 HARV. INT'L L. J. 353 (2006); *see also* Cyrill P. Rigamonti, *The Conceptual Transformation of Moral Rights,* 55 AM. J. COMP. L. 67 (2007).

[562] Such agreement provides an opportunity for the IND/CTA applicant to insist that all its costs up to the stage of IND/CTA application has to be reimbursed by the drug originator.

test the said molecule through human trials for a certain time period. Within this period, it must either commence the trials by itself or elect to have its INDA approval acted upon, and the molecule taken through clinical testing by an interested third party. During this period of protection, the regulator shall not entertain any IND/CTA application covering the same drug from any other firm.

In other words, the regulator shall not entertain any other IND/CTA application for the same drug until such time as the trials are completed by either the IND applicant or an interested party as above mentioned. If the drug is finally approved, the restriction on the ability of a third party to manufacture a follow on drug continues, in view of the investment protection regime advocated in this thesis.

A conditional IND/CTA right operates as an additional incentive to small biotechnology firms, universities, public funded research institutions and other entities who might have sufficient resources and expertise to file an IND/CTA application, but not enough to take a molecule through human trials.[563] The incentives include not only the prospect of recovery of costs, but also that of a joint right of paternity to be identified as a drug originator along with the firm that finally procures drug regulatory approval. It bears noting that the aspects relating

[563] Kneller found that small biotechnology firms that either made upstream discoveries or acquired such upstream discoveries from universities themselves filed the new drug application (NDA) in 60% of the cases (51 out of 86 drugs that were studies). The remaining 40% were cases where the drug was taken to trial by another firm, mainly those with deep pockets. Kneller, *supra* note 550.

to recovery of costs by the IND/CTA applicant from the final drug developer would depend largely on the contractual terms between them. Further, the drug regulator ought not to disclose the molecule/substance comprising the prospective drug in question, but merely that it allegedly helps with a certain disease and the relevant contact information of the IND/CTA applicant. This information should be sufficient to entice prospective drug developers in directly approaching the IND/CTA applicant and negotiating a contract with them; which would presumably include obligations to keep information revealed by the IND/CTA applicant confidential.

An added advantage of this model is that by conferring a limited first right to conduct trials based on the IND/CTA filing, wasteful expenditures generated out of competitive races are avoided, where multiple firms work on the same drug molecule and file similar submissions before the drug regulatory authority.[564]

**2. Trade Secrecy**

[564]*See* Roin, *supra* note 2, at 568 (noting the problem of wasteful races in the context of the current drug regulatory and data exclusivity regimes). He notes:

> The only significant problem with the FDA-enforced exclusivity periods is that they might permit wasteful development races in clinical research, but this problem could be avoided. If no single firm is given the exclusive rights to develop a drug, multiple competing firms could decide to run clinical trials on it at the same time in the hopes of being the first to receive FDA approval. The FDA could easily prevent such races, however, because firms cannot begin testing a drug in clinical trials without the FDA's approval, so the FDA could give its approval to only one firm.

An upstream third party invention could be protected as a trade secret, [565] whereby the inventor discloses it to others only under a contract of confidentiality, which stipulates the terms of disclosure.[566] It is possible that, apart from standard royalty terms, the agreement also stipulates that the final drug originator take into account the costs of the upstream inventor, whilst submitting its costs for the purpose of claiming reimbursement under the investment protection regime, as prescribed in this thesis.

The key advantage of a trade secrecy regime is that protection is automatic in nature and there are no costs or formal registration processes, as with patents. Secondly, unlike patents, trade secrets are potentially of infinite duration and they last until such time that the secrets are independently discovered by a third party. Such independent discovery might occur in two ways. The first is the classic case of reverse engineering, where a product embodying the trade secret is placed in the market and the said product is 'pried open' to discover the underlying idea. The second is where the same idea occurs independently to a third party.

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[565] Trade secrets are protected in many countries, either through a statutory enactment or by way of common law. The Uniform Trade Secrets Act (USTA) in the US defines trade secret as that which (1) derives independent economic value, actual or potential, from not being generally known to and not being readily ascertainable by proper means by, other persons who can obtain economic value from its disclosure or use and (2) is the subject of efforts that are reasonable under the circumstances to maintain its secrecy. Uniform Trade Secrets Act § 1(4), 14 U.L.A. 372 (Supp. 1989); *see also* Robert Graham Gibbons & Bryan J. Vogel, *The Increasing Importance of Trade Secret Protection in the Biotechnology, Pharmaceutical and Medical Device Fields*, 89 J. PAT. & TRADEMARK OFF. SOC'Y 261, 264 (2007).

[566] Any breach of such contract by any of the parties thereto could, apart from attracting sanction under the relevant trade secrecy regime, also entail consequences under the relevant law of contract.

The prospect of reverse engineering playing out in the drug discovery context is rather remote, given that the upstream discoverer is not likely to have any product embodying the idea.[567] Rather, in most cases, the discovery would have to be tested and developed into a marketable product (approved drug) through an expensive and time-consuming process that lasts several years from the time when the upstream inventor first came up with the discovery.

Secret upstream inventions could be independently discovered by a third party. However, the scope for such independent discovery depends in part on how "inventive" or "non-obvious" the idea is. If the idea is relatively more obvious, it has a higher chance of being independently discovered. And if less obvious, it is likely to escape independent discovery for a longer period of time. However, if less obvious, the idea also has a greater prospect of being registered as a patent. In such a case, the upstream inventor will have to choose between patent protection and trade secrecy protection.

### 3. Publications, Reputational Gains and Collaborative Innovation

[567] This proposition holds good for new pharmaceutical processes as well, and a trade secrecy regime could help protect such processes from unauthorised disclosure and use.

Apart from the prospects of being protected through trade secrecy and a limited IND right, upstream incentives may also come in the form of reputational gains[568] and publication prospects, particularly to those working in academic and research institutions. It is likely that such research institutions are recipients of public funding that permit their researchers to continue discovering new ideas without the need for any other external monetary incentive.

The Open Source Drug Discovery (hereinafter "OSDD") project by the Indian Council for Scientific and Industrial Research (hereinafter "CSIR") is an attempt to leverage non-patent incentives at the upstream level by *inter alia* fostering collaborative and open innovation between different researchers across the world who come together in their quest to find a cure for tuberculosis (hereinafter "TB").[569] Specific credits are offered to those participants who make valuable suggestions, and this serves as a good reputational non-patent incentive, an aspect that will be more elaborately discussed in Chapter VIII dealing with alternative innovation incentives.

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[568] This holds especially true for open source software. Stephen Maurer, *The Right Tool(s): Designing Cost-Effective Strategies for Neglected Disease Research* 23 (Mar. 29, 2005) http://www.who.int/intellectualproperty/studies/S.Maurer.pdf.

[569] The OSDD project deploys an online social networking platform to leverage the expertise of several scientists and students across the globe and arrive at a potential cure for TB. The participants in the OSDD consist of students, scientists, researchers, academicians, institutions, corporations and anyone else committed to the ideology of discovering drugs in an open collaborative mode. Open Source Drug Discovery, *About Us*, *available at* http://www.osdd.net/about-us (last visited Sept. 28, 2011); *see also* discussion in Chapter VIII, *infra* text accompanying notes 789-792.

The above discussion points to the existence of a number of potential incentives to foster upstream invention by third parties. Given that there are significant non-patent incentives that could be availed of to ensure that upstream pharmaceutical research (by third parties) continues without serious disincentive, patent standards for upstream inventions could be kept at fairly high thresholds,. This point is an important one to appreciate, given the proliferation of 'me-too' drugs[570] involving the deliberate gaming of the patent system to extend monopolies by effectuating inconsequential changes to existing molecules.

Further, given that patents over upstream inventions have the potential of blocking down downstream drug development,[571] countries could also institute wide experimental use exceptions and compulsory licensing provisions, an aspect dealt with in detail below.[572]

### B. Experimental Use Exception

As the name suggests, an experimental use exception shields experimental activities from charges of patent infringement. The underlying rationale of such an exception is that experimentation on a patented invention is necessary to test the

[570] *See* discussion in Chapter IV: Investment Protection Regime *supra* text accompanying notes 451-453.

[571] *See* Heller & Eisenberg, *supra* note 92, at 698-701.

[572] Although there are several other limitations and exceptions under patent law that countries could strategically leverage to foster national innovation policy and public health goals, I discuss only two of the most prominent ones, namely experimental use and compulsory licensing.

invention and ensure that it works in the manner claimed.[573] Some countries have gone further and permitted the use of such an exception to even cover the testing of patented inventions with a view to creating improvements or inventing around such patents.[574]

The existence and extent of the "experimental use" exception has been the subject of several scholarly debates the world over. A broad interpretation of the experimental use exception would permit the "use" of a patented invention to: [575]

(i) develop follow-on inventions and improvements; and

(ii) invent around or design around the patented invention.

Proponents of the "broad" school of thought argue that access to "patented information" *per se* would be of little use, unless it could be used in meaningful ways to advance the technological arts.[576] The above argument is further buttressed by the fact that most patent law regimes expressly or impliedly provide for the patenting of improvements. A broad "experimental use" exception is likely

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[573] *See* Shamnad Basheer & Prashant Reddy, *The "Experimental Use" Exception Through a Developmental Lens'* 50 IDEA 831, 833 (2010).

[574] *See id.* at 833.

[575] Contrast this with a narrow interpretation, which would suggest that in most cases, a researcher is only permitted to test the patented invention for purely philosophical purposes i.e. to understand the underlying invention and to repeat its working etc. *id*. at 841.

[576] *See id.* at 840.

to spur the progress of science and technology, without detracting significantly from the incentives of the patentee to invent in the first place.[577]

Consider the example of *Merck KGaA v. Integra LifeSciences I Ltd.*[578], where Merck was sued by Integra for conducting pre-clinical research on a compound patented by Integra. Merck sought refuge under the "safe harbour" *Bolar* exception, which exempts from patent infringement all such activities aimed at securing regulatory approval from the U.S. FDA.[579] The Federal Circuit interpreted the *Bolar* provision rather narrowly, stating that the phrase "reasonably related" could not be expanded to include all stages of drug development; rather, only those activities which directly resulted in the submission of information to the FDA would be covered. On appeal, the U.S. Supreme Court reversed this decision, holding in favour of a broad interpretation of the 'safe harbour' provision, stating that any upstream activity that could result in the submission of information to the FDA is covered by the *Bolar* provision.[580]

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[577] *See id.*

[578] Integra had sued Merck for the infringement of its patents numbered 4,988,621, 4,792,525, 5,695,997, 4,879,237 and 4,789,734. All the patents were related to a short tri-peptide segment of fibronectin having the sequence Arg-Gly-Asp. The District Court turned down Merck's defense on the basis that it was covered by the "Bolar" exception. Merck KGaA v. Integra LifeSciences I Ltd, 545 U.S. 193 (2005); *see also* Integra LifeSciences I Ltd. v. Merck KGaA, 50 US PQ 2d 1846 (S.D. Cal. 1999).

[579] *See* Integra Lifesciences I, Ltd. v. Merck KGaA, 331 F.3d 860 (Fed. Cir. 2003).

[580] *See* Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 207 (2005).

Had the Supreme Court endorsed the Federal Circuit ruling, Integra could have used its upstream patent to block Merck's downstream product. This case illustrates the value of having a wide experimental use exception in the drug development context.[581]

Such a broad application of the experimental use exception as advocated in this thesis is not likely to violate TRIPS either. Article 30 of TRIPS, the key provision dealing with patent exceptions states:

> [M]embers may provide limited exceptions to the exclusive rights conferred by a patent, provided that such exceptions do not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties.[582]

An exception that permits the use of a patented invention only for the purpose of experiment or research or education is likely to be seen as a 'limited' exception. Further, even assuming that this impacts the 'normal' exploitation of a patent to some extent, it does not do so 'unreasonably.' A study of the underlying technology with a view towards improving the patented technology, or to invent around it cannot be said to be an unreasonable interference with the normal exploitation of a patent. If that were the case, patents would end up blocking the advancement of

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[581] *See* Jennifer Miller, *Sealing the Coffin on the Experimental Use Exception*, 2 DUKE L. & TECH. REV. 1-9 (2003) (explaining that in the wake of the Madey v. Duke decision, many opined that there is no real experimental use exception in the U.S.; the Supreme Court had to work within the bounds of the Bolar provision, a provision aimed only at exempting activities tied in to FDA submissions).

[582] *See* TRIPS, art. 30.

science and technology, the very purpose for which they were instituted in the first place. Such a reading would also be at odds with the disclosure function of patents.[583] For the same reasons as above, it is likely that a WTO panel would find that the experimental use exception does not unreasonably prejudice the "legitimate" interests of a patent owner.[584]

However, in order to effectively leverage this exception in the broad manner as suggested, states must ensure that there is a complete and enabling disclosure of the patented invention. This would not only ensure that patentees live up to their part of the bargain and merit the 20 year monopoly that society grants them, but also help a number of inventors to study patents effectively, and experiment with underlying technology.[585]

In short, states could incorporate wide experimental use exceptions in their regimes to ensure that upstream inventions do not pose an obstacle for downstream drug development.

### C. Compulsory Licensing

[583] *See* Basheer & Reddy, *supra* note 573, at 864.

[584] *See id.*

[585] *See id.* at 872

A robust experimental use exception is likely to shield the use of an upstream (patented) invention to help discover a drug candidate or to develop that candidate into a marketable drug. However, once the drug has been approved by the regulator and is ready for marketing, the drug originator cannot manufacture and sell it without the permission of the upstream patentee. In order to reduce the scope for blocking in such a context,[586] countries could institute compulsory licensing norms.[587]

It bears noting that the Indian patent regime contains some of the widest grounds for the issuance of compulsory licenses. § 84 of the Indian Patents Act, 1970 stipulates that after three years from the date of grant of a patent, a compulsory licence could be applied for by any person on the following grounds:[588]

i. that the patented product is excessively priced in the market[589];

ii. that the reasonable requirements of the public with respect to the

[586] *See supra* text accompanying notes 94-96.

[587] *See supra* note 6.

[588] The contours of the term "reasonable requirements" of the public as used in § 84 is spelt out in § 84(7) which illustrates situations where the reasonable requirements of the public will not be deemed to have been met. These include: i) where an applicant proves that an existing trade or industry is prejudiced by the operation of a certain patent; ii) where a market for export of the invention manufactured in India is not being "supplied or developed" or a scenario where the establishment or development of commercial activities in India is prejudiced; iii) where the "demand for the patented article has not been met to an adequate extent or on reasonable terms" is also included in this provision.; and iv) certain anti-competitive practices such as patent licences which impose a condition of "exclusive grant back," "prevention to challenges to the validity of a patent" or "coercive package licensing."

[589] *See* The Patents Act, No. 39 of 1970, INDIA CODE (1999), § 84(1)(a).

patented invention have not been satisfied[590]; and

iii. that the patent has not been worked in India.[591]

Further, § 91 addresses the situation of "blocking patent" by stating that any patentee who is unable to work his/her invention without infringing an earlier registered patent may apply for the grant of a compulsory licence.[592] Under this provision, any person who improves upon a patented technology and subsequently registers such improvement as a patent can apply for a compulsory licence to work the improvement without infringing the original patent. In a report that formed the basis of the current Indian patent regime, the rationale for such a provision was explained thus:

> One of the common types of abuses of patent monopolies is the use of patents for blocking purposes i.e. "putting the patented invention on ice" while others are prepared and desirous of working them. The provisions of this clause would effectively counter any tendency to resort to such a form of abuse.[593]

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[590] *See* The Patents Act, No. 39 of 1970, INDIA CODE (1999), § 84(1)(b). For a parallel provision, see Patents Act, 1977 § 48A(1)(a) (Eng.). One form of this could be when the patented product is not available in adequate quantities in the market; *see also* discussion *supra* note 396-397 and accompanying text.

[591] *See* The Patents Act, No. 39 of 1970, INDIA CODE (1999) § 84(1)(c).

[592] *See* The Patents Act, No. 39 of 1970, INDIA CODE (1999) § 91, It reads:

> Notwithstanding anything contained in the other provisions of this Chapter, at any time after the sealing of a patent, any person who has the right to work any other patented invention either as patentee or as licensee thereof, exclusive or otherwise, may apply to the Controller for the grant of a licence of the first mentioned patent on the ground that he is prevented or hindered without such licence from working the other invention efficiently or to the best advantage possible.

[593] *See* JUSTICE N. RAJAGOPALA AYYANGAR, REPORT ON THE REVISION OF THE PATENTS LAW 231 (1959) http://www.spicyip.com/docs/Rajagopala_Ayyangar_Report/Rajagopala_Ayyangar_Report_1-20.pdf

The key limitation of this provision is that it only applies to situations where the subsequent improvement is patented and cannot be availed of by third parties who make unpatented improvements to patented technologies, no matter how significant such improvements are to the technological field in question.

Secondly, the provision can only be availed of, if the improver herself is willing to grant a license back to the original patent owner.[594] There is no reason why a WTO member state cannot expand such a ground to include all instances where the patent effectively blocks the evolution of an improvement, an aspect discussed later in this Chapter.

The U.K. regime has provisions that are largely similar to that of India, albeit of a narrower scope.[595] The regime is unique, in that it bifurcates licensing grounds depending upon whether the patent is owned by a proprietor from a WTO member country or not.[596] § 48A of the U.K. Patents Act, 1977 deals with patents belonging to applicants from WTO member states and stipulates that licenses in respect of such patents can be obtained on 3 grounds:

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[594] *See* The Patents Act, No. 39 of 1970, INDIA CODE (1999) §91(2) which deals with the conditions under which the Controller may grant a licence under § 91(1); *see also* § 91(2)(i) (providing that the applicant must be willing to enter into an agreement akin to a cross-licensing agreement, in which the applicant must grant the rights to work her patent to the person/entity under whose patent she has filed the application under § 91(1)).

[595] *See* Patents Act, 1977 §§ 48A & B (Eng.)

[596] *See id.*

(i) Where the demand for the patented invention in the U.K. is not being met on reasonable terms;

(ii) Where the refusal of a voluntary licence on reasonable terms, prevents or hinders, the exploitation in the U.K. of any other patented invention which involves an important technical advance of considerable economic significance;

(iii) Where the conditions imposed either on the grant of licences for the patent or the use of the patent itself, unfairly prejudices the development of any industry or the use of any product not covered by any patent.

All of the above grounds discussed so far (from both the Indian and U.K. regimes) could be broadly conceptualised as grounds triggered by an act or omission on the part of the patentee. Some of these acts or omissions might even be categorized as an 'abuse', which is an act contrary to the larger public interest.[597]

Apart from this, WTO member states also provide for compulsory licenses in situations that bear no nexus to the conduct or omission of the patentee. Illustratively, the Indian regime provides that compulsory licenses could be granted to tackle public health epidemics such as AIDS, malaria and tuberculosis.[598] Such

[597] *See S*hamnad Basheer & Mrinalini Kochupillai, *Compulsory Licensing Regime in India: Past, Present and Future* 12-13 (Jul. 1, 2005) http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1685129.

[598] *See*, The Patents Act, No. 39 of 1970, INDIA CODE (1999) § 92.

grounds could be broadly categorized as public interest grounds.[599] These grounds (both abusive and public interest oriented) find resonance in the patent regimes of many WTO countries.[600]

Given that TRIPS does not circumscribe the grounds for compulsory licensing, member states are free to articulate their own grounds. However, whatever the chosen grounds, member states are to comply with the procedural pre-requisites laid down by TRIPS, such as the fact that the applicant must first negotiate a voluntary licence with the patentee prior to seeking a compulsory licence, unless the patent is required in a case of an emergency or a national urgency.[601] Article 31 of TRIPS spells out the remaining threshold requirements for the use of a patent without the authorisation of the rights holder.

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[599] *See* Basheer & Kochupillai, *supra* note 597, at 12.

[600] For instance, Article 43 of the Japanese Patent Law allows for compulsory licensing if a patent is not worked, sufficiently and continuously, for at least three consecutive years after it has been granted. Patent Act, Law. No. 121 of 1959)(Japan); Germany too, allows compulsory licences if the patent is not worked within three years of the grant. § 24 of German Patent Law allows for the grant of compulsory licences if the 'public interest' requires it to be issued. The same provision also states that compulsory licences maybe issued to ensure the 'adequate supply' of the patented product to the domestic market in Germany. German Patent Law, December 16th 1980 (Ger.); As per § 65 of Canadian Patent Law, a compulsory license may be granted three years after the grant of the patent if, "the demand for the patented article in Canada is not being met to an adequate extent and on reasonable terms." Patent Act, 1985 (Can.); Art. L.613-11 of French Patent Law allows for the grant of compulsory licence within three years of grant of patents if the patentee is not adequately working the patent or if the patented invention is not available in France in sufficient quantities. Intellectual Property Code (Fr.), art. L. 613-11; Art. 68, of Brazil's Patent law, allows for the grant of compulsory licensing for the failure to exploit the patent on Brazilian territory or in the case of 'commercialization that does not satisfy the needs of the market'. Brazil – Law No. 9,729, of May 14, 1996; *see generally* Jerome Reichman, *Compulsory Licensing of Patented Inventions: Comparing United States Law and Practice with Options under the TRIPS Agreement*, 1 (AALS Mid-Year Workshop on Intellectual Property, Vancouver, Canada, June 14-16, 2006) , *available at* http://www.aals.org/documents/2006intprop/JeromeReichmanOutline.pdf.

[601] *See* TRIPS, art. 31.

Although countries have wide latitude in devising the grounds for issuance of compulsory licenses, it would appear that there are limits to this latitude. Member states may not be able to institute a blanket or 'groundless' compulsory licensing regime and remain compliant with TRIPS. The term 'groundless, is used to merely refer to the fact that a compulsory licence is issued, without the need to demonstrate the existence of any specific 'ground'.

Article 31(a) of TRIPS states that compulsory licences have to be issued on a case-by-case basis. This could be taken to indicate that a groundless or a blanket compulsory licensing regime might not pass muster under TRIPS. Further, the TRIPS negotiating history shows that India attempted to advocate for a recognition of its own 'licence of right' regime, whereby certain kinds of technologies, such as food and medicines, were subject to automatic or blanket compulsory licensing, without any reference to specific grounds.[602] However, the TRIPS Council members refused to adopt this, indicating thereby, that blanket compulsory licences without reference to patentee conduct or other specific grounds might not be compatible with TRIPS.[603]

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[602] *See* Cynthia M. Ho, *On Breaking Patents: Separating Strands of Fact from Fiction under TRIPS*, 22 (Sep. 2008), *available at* http://works.bepress.com/cgi/viewcontent.cgi?article=1001&context=cynthia_ho ; *see also* Janice M. Mueller, *The Tiger Awakens: The Tumultuous Transformation of India's Patent System and the Rise of Indian Pharmaceutical Innovation*, 68 UNIV. PITTS. L. REV. 491 (2007).

[603] *See* Ho, *supra* note 602, at 22; *see also Standards and Principles Concerning the availability, Scope and Use of Trade-Related Intellectual Property Rights- Communication from India* (Jul. 10, 1989), MTN.GNG/NG11/W/37 (proposing licenses of right for food, pharmaceuticals and chemicals

Based on the above, one might suggest that a blanket or groundless compulsory licence might contravene TRIPS. However, countries have wide latitude in crafting a wide array of specific grounds to trigger compulsory licenses and thereby ensure that upstream patents do not block the prospects of downstream drug development.

separate from individualized review of compulsory licenses, with no opportunity for administrative or judicial review).

## CH. VII: INNOVATION POLICY FROM A GLOBAL PERSPECTIVE

The central argument of this thesis is that an investment protection regime is a more optimal policy incentive for fostering higher levels of investment in drug discovery and development than existing patent and data exclusivity regimes. The issue of incentives has to be examined from a global perspective and this would necessarily entail dealing with all countries, developed, developing and least developed.

### A. IP and Development

It is a well-established fact that pharmaceutical R&D is unevenly distributed throughout the globe, with the U.S., EU and Japan accounting for the largest share.[604] Further, the main markets for most drugs are located in these very jurisdictions.[605] The incentive of an investment protection regime works optimally

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[604]This study found that of a total of 1400 first-year pharmaceutical patents granted between 2000-09, the inventors were concentrated mainly in the US, Europe and Japan *i.e.* "60% of inventors were from the United States and 31.5% of inventors from Europe (United Kingdom, Germany, Sweden, France, Switzerland and Belgium) and Japan. Yali Friedman, *Location of Pharmaceutical Innovation: 2000-2009*, 9 NATURE REVIEWS DRUG DISCOVERY 835 (2010); *see also* Kevin Outterson, *Patent Buy-Outs for Global Disease Innovations for Low- and Middle-Income Countries*, 32 AM. J. L. & MED. 159, 160 (2006).

[605] *See* Friedman, *supra* note 604, at 835 ("The United States is the world's largest pharmaceutical market, comprising roughly 40% of the world's pharmaceutical revenues. Accordingly, the majority of pharmaceuticals developed worldwide would be expected to be marketed in the United States."); *see also* WORLD HEALTH ORGANISATION, INTELLECTUAL PROPERTY RIGHTS, INNOVATION, AND PUBLIC HEALTH, WORLD HEALTH ASSEMBLY RES. WHA56.27 10TH PLEN. MTG. (2003) (reporting that the World Health Assembly estimates that approximately 90% of drug sales are in developed countries); *see also* G KUMARA ET AL., MCKINSEY & CO., INDIAN PHARMA 2015: UNLOCKING THE POTENTIAL OF THE INDIAN PHARMACEUTICALS MARKET 11 (2007), *available at* http://www.mckinsey.com/locations/india/mckinseyonindia/pdf/India_Pharma_2015.pdf (predicting that the US, Japan and certain European countries, would continue to remain the top

in such developed countries. However, what of developing and least developed countries such as Kenya and Bangladesh? Should similar investment protection regimes be implemented within such jurisdictions as well? Would the institution of investment protection regimes in these countries (which are effectively net importers of technology goods) detrimentally impact the innovation and public health goals of such countries by preventing them from learning by imitation? If these countries fail to institute regimes similar to the U.S., EU and Japan, would this hamper the rate of global innovation? Unfortunately, we do not have any conclusive answers in this regard. The advent of TRIPS triggered a number of scholarly papers and commentaries on this issue, now widely subsumed under the rubric of the "IP and development" theme.[606]

This theme intensified to such an extent that the World Intellectual Property Organisation (hereinafter "WIPO"), an organisation that for years perpetuated the dogmatic belief that higher levels of IP protection always translated to greater economic development, was forced to acknowledge and accept a 'development

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pharmaceutical markets even in 2015, despite the extremely fast growth in emerging markets like India & Brazil; more specifically, the report predicts that in 2015, the US will be valued at U.S. $444 billion, followed by Japan at U.S. $82 billion, France at U.S. $47 billion and Germany & China equally placed at U.S. $38 billion).

[606] *See generally* THE DEVELOPMENT AGENDA: GLOBAL INTELLECTUAL PROPERTY & DEVELOPING COUNTRIES (Neil Weinstock Netanel ed., 2009)*; see also* Margaret Chon, *Intellectual Property & the Development Divide*, 27 CARDOZO L. REV. 2821 (2006); *see also* Peter K. Yu., *A Tale of Two Development Agendas*, 35 OHIO N.U. L. REV. 465 (2009); *see also* Jeremy De Beer & Sara Bannerman, *Foresight into the Future of WIPO's Development Agenda*, (2010) 1 W.I.P.O.J. 211.

agenda.' This agenda advocated by a group of developing countries[607] is premised on the logic that intellectual property protection must be calibrated according to the specific technological capabilities and economic wealth of the country in question.[608]

The key issue for a number of developing and least developed countries which do not produce any drugs of their own, but import them from other countries, is: What national advantage will they gain by providing protection through patents and other market exclusivities, when such protection works largely in favour of multinational pharmaceutical firms that use them to import and sell drugs at monopoly prices? Would the denial of patents and other exclusivities in these poor developing countries harm the future of global pharmaceutical

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[607] *See* Carolyn Deere, *WIPO Development Agenda: Developing Countries Submit New Proposals,* INTELLECTUAL PROPERTY WATCH, (Apr. 6, 2005),http://www.ip-watch.org/weblog/2005/04/06/wipo-development-agenda-developing-countries-submit-new-proposals/ ("The Friends of Development Group comprises the co-sponsors of the original proposal to establish a WIPO "Development Agenda" (Argentina, Bolivia, Brazil, Cuba, Dominican Republic, Ecuador, Egypt, Iran, Kenya, Peru, Sierra Leone, South Africa, Tanzania and Venezuela).").

[608] The proposal by Argentina and Brazil for the establishment of a 'development' agenda castigates WIPO for its "one size fits all" philosophy and asks it to be sensitive to the fact that countries with differing levels of development require different kinds of IP policies. The proposal argues that the incorporation of a development dimension into WIPO's outlook will only serve to strengthen the credibility of the IP system. WORLD INTELLECTUAL PROPERTY ORGANISATION, PROPOSAL BY ARGENTINA AND BRAZIL FOR THE ESTABLISHMENT OF A DEVELOPMENT AGENDA FOR WIPO, Doc. No. WO/GA/31/11 (2004); *see also* Haochen Sun, *The Road to Doha and beyond: Some Reflections on the TRIPS Agreement and Public Helath,* 15(1) E.J.I.L. 123 (2004); *see also* Nadia Natasha Seeratan, *The Negative Impact of Intellectual Property Patent Rights on Developing Countries: An Examination of the Indian Pharmaceutical Industry,* 3 SCHOLAR 339 (2001).

innovation? Would there be some danger of a collective action problem?[609] I deal with this issue both from a national perspective as also an international one.

From the perspective of national innovation policy and strategy, many scholars suggest that countries that are net importers of technology are better off without strong IP or market exclusivity enhancing regimes.[610] Rather, narrower monopolies leave more scope for technological growth through learning and imitation.[611] Further, it would reduce the prospects of the country remaining dependent on high priced foreign imports.[612] This dependence is particularly problematic for poor developing countries, where issues of drug pricing and access

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[609] *See* B Pazderka & K Stegemann, *Pharmaceutical Innovation as a Collective Action Problem: An Application of the Economic Theory of Alliances*, 8(2) J. W. INTEL. PROP. 157 (2005).

[610] *See* Basheer & Primi, *supra* note 401, at 100.

[611] *See generally* S. Chaudhuri, *Is Product Patent Protection Necessary in Developing Countries for Innovation: R&D by Indian Pharmaceutical Companies after TRIPS* (Indian Institute of Management Working Paper No. 614, 2007), *available at* http://203.197.126.103/res/upd%5CSudip%20Wp%20614.pdf; *see also* Brian Casey, *Perspectives on the Patent system and its Role in Innovation: A Way Forward?,* 4 OTAGO MANAGEMENT GRADUATE REVIEW 2, 2 (2006), *available at* http://www.business.otago.ac.nz/mgmt/research/omgr/06casey.pdf ("One of the more obvious benefits supposed to accrue from the weak protection of intellectual property, especially for developing countries, is claimed to be the cheap acquisition of technology through imitation, and the encouragement this provides to innovation"); *see also* EDITH TILTON PENROSE, THE ECONOMICS OF THE INTERNATIONAL PATENT SYSTEM (1951); *see also* Douglas F. Geer, *The Case Against Patent Systems in Less-Developed Countries*, 8 J. INT'L L. & ECO. 223 (1973).

[612] *See* KEITH MASKUS, PETERSON INSTITUTE OF INTERNATIONAL ECONOMICS, *Intellectual Property Rights and Economic Development: Patents, Growth and Growing Pains*, *in* INTELLECTUAL PROPERTY RIGHTS IN THE GLOBAL ECONOMY 143, 159 (2000), *available at* http://www.piie.com/publications/chapters_preview/99/5iie2822.pdf ("A major concern of technology importers is that strong patents...expand the market power of foreign providers of information and new products, permitting high price mark-ups. In turn, importing countries would experience losses in their terms of trade, while access to new products and key inputs could be diminished.").

to medicines[613] are more accentuated.[614] As already noted in Chapter IV, patent exclusivities have the potential to trigger extremely high prices.[615] A commentator notes:

> The patent-based pharmaceutical R&D and distribution systems in high income countries function as well as they do in large part because of elaborate and expensive subsidy and social insurance mechanisms. Poorer countries generally lack these resources. They cannot afford multi-billion dollar NIH style grant programs to focus attention on local health conditions. They do not subsidize the cost of the vast array of patented medicines to the point where they are affordable. Their citizens are much poorer and cannot afford most patented medicines. Global pharmaceutical markets simply do not work as well for the world's non-wealthy people, perhaps 85% of humanity.[616]

Therefore, developing countries may be better off in strategically tailoring their intellectual property regimes to leave more scope for technological imitation and to reduce their dependence on excessively priced imports. The success of such tailoring strategy is borne out by historical evidence, where several countries

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[613] *See* U.S. DEPARTMENT OF COMMERCE, *Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation*, 3 (December, 2004) http://www.ita.doc.gov/td/chemicals/drugpricingstudy.pdf (suggesting that in wealthier developed countries, on the other hand, access issues are ameliorated by government-subsidized insurance and other social mechanisms).

[614] *See* Jean O. Lanjouw & William Jack, *Trading Up: How Much Should Poor Countries Pay to Support Pharmaceutical Innovation?,* 4(3) CGD BRIEF 1 (2004), *available at* http://www.cgdev.org/files/2842_file_CGDbrief_pharmaceutical.pdf; *see also* Rajat Khosla & Paul Hunt, *Human Rights Guidelines for Pharmaceutical Companies in Relation to Access to Medicines*, http://www.essex.ac.uk/human_rights_centre/research/rth/docs/Final_pharma_for_website.pdf (estimating that more than 2 billion people are effectively priced out of the market for patented drugs drawing from his experience as a former UN Special Rapporteur on the right to the highest attainable standard of health).

[615] *See* discussion on the Makena and Colchicine examples in Chapter IV: Investment Protection Regime *supra* text accompanying notes 487-394**.**

[616] *See* Outterson, *supra* note 554.

deliberately instituted weak IP regimes in the past to promote more technological imitation, before moving on to stronger IP regimes. Illustratively, Japan did not provide patent protection for chemical and pharmaceutical products until 1976,[617] Italy until 1978[618] and Spain until 1992.[619] Other European countries like West Germany and Switzerland did not provide for pharmaceutical patent protection until the years 1967 and 1978 respectively.[620]

The most recent example is that of India,[621] which did away with patent protection for pharmaceutical products in 1970, owing to the findings of a Committee that the patent system was being exploited by multinational companies, particularly in relation to vital industries such as food, chemicals and

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[617] *See* Reiko Aoki & Tomoko Saiki, *Implications of Product Patents – Lessons from Japan,* 3 (Commission on Intellectual Property Rights, Innovation and Public Health Study, April 2005), *available at* http://www.who.int/intellectualproperty/studies/R.Aoki.pdf; *see also* Hisamitsu Arai, *The "Intellectual Creation Era" Will Shine on Asia* (Sept. 10-12, 1997), http://www.jpo.go.jp/cgi/linke.cgi?url=/shiryou_e/toushin_e/kouenroku_e/kichoe.htm.

[618] *See* Livio Garattini & Simone Ghislandi, *Off-patent Drugs in Italy: A Short-sighted View?*, 7(1) EUR. J. HEALTH ECON. 79, 80 (2006).

[619] *See* MICHELE BOLDRIN & DAVID K. LEVINE, *The Pharmaceutical Industry, in* AGAINST INTELLECTUAL MONOPOLY 241, 245 (2008), *available at* http://levine.sscnet.ucla.edu/papers/ip.ch.9.m1004.pdf (noting that in Spain product patents were introduced in 1986 just after its accession to the European Economic Community (EEC) but the laws were made effective from 1992); *see also* Mohammad M. Azam & Kristy Richardson, *Pharmaceutical Patent Protection and TRIPS Challenges for Bangladesh: An Appraisal of Bangladesh's Patent Office and Department of Drug Administration,* 22(2) BOND L. REV. 1, 4 (2010), *available at* http://epublications.bond.edu.au/cgi/viewcontent.cgi?article=1389&context=blr (citing Xuan Li, *The Impact of Higher Standards in Patent Protection for Pharmaceutical Industries under the TRIPS Agreement-A Comparative Study of China and India*, (2008) THE WORLD ECONOMY 1368).

[620] *See* Xuan Li, *The Impact of Higher Standards in Patent Protection for Pharmaceutical Industries under the TRIPS Agreement-A Comparative Study of China and India*, 1 (United Nations University-World Institute for Development Economic Research, Research Paper No. 2008/36, April 2008), *available at* http://www.wider.unu.edu/stc/repec/pdfs/rp2008/rp2008-36.pdf ("In Germany, product patents were explicitly excluded under the law of 25 May 1877 but were then introduced from 4 September 1967...[i]n Italy pharmaceutical patents were prohibited until 1978").

[621] *See id.* at 5.

pharmaceuticals.[622] Foreign patentees used their patents to keep out competition and charged excessively high prices for imported products. The Committee, therefore, recommended that certain inventions relating to vital products (i.e. drugs, chemicals and food) be granted only process patent protection. India's well-developed generic industry today is testimony to the prescience of this report.[623]

Much in line with this traditional wisdom, developing countries may wish to implement a similar innovation policy that permits a significant amount of technological learning and imitation prior to adopting a strong IP regime. Unfortunately, owing to the advent of TRIPS which mandates a minimum level of protection for all inventive products and processes (including pharmaceuticals), developing countries do not have the same range of flexibilities anymore.[624]

It is important to appreciate in this context that developing countries are not one monolithic block, but amenable to further categorisation based on levels of technological proficiency and economic development. In a paper written some years ago, I cautioned:

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[622] *See* JUSTICE N. RAJAGOPALA AYYANGAR, REPORT ON THE REVISION OF THE PATENTS LAW (1959), *available at* http://www.spicyip.com/docs/Rajagopala_Ayyangar_Report/Rajagopala_Ayyangar_Report_1-20.pdf.

[623] *See* Shamnad Basheer, *India's Tryst with TRIPs: The Patents (Amendment) Act, 2005,* 1 IND. J. LAW & TECH. 18 (2005).

[624] *See* TRIPS, art. 27 (stating that "patents shall be available and patent rights enjoyable without discrimination as to the place of invention, the field of technology and whether products are imported or locally produced.").

> We need to …. move away from an antiquated developed-versus-developing classification and differentiate developing countries according to their technological/innovative proficiencies. Such differentiation would help calibrate IP norms according to the specific developmental needs of the country in question. The evolution of the BRICS group might represent the first stage in this process of differentiation among developing economies…..[625]

The paper went on to label BRIC countries such as India as 'technologically proficient developing countries'[626] and argued that these countries may have different development imperatives than their technologically poorer counterparts.[627]

## B. IP and Global Innovation

The above discussion centred on optimal IP and innovation policy from a national perspective. However, what of global innovation imperatives? In other

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[625] *See* Basheer & Primi, *supra* note 401.

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> India is neither developed nor developing. India has a rapidly growing economy, and strength in its technology sectors—such as software and pharmaceuticals—bestows upon India some developed-country characteristics. On the other hand, India's Human Development Index ranks as one of the lowest in the world. Over one-quarter of its people live below the poverty line, which keeps India from fully transcending its developing-country status.

Basheer & Primi, *supra* note 401, at 101.

[627]

> [T]he argument that developing countries always ought to implement the lowest level of protection mandated under the TRIPs Agreement is not a sound one. To this extent, one ought to appreciate that what is compliant with the TRIPs Agreement and what is good from a national policy perspective are two different issues and one ought not to conflate them. Thus, although India was not mandated by the TRIPs Agreement to grant data exclusivity to traditional medicines, it saw the need to do so from a national policy perspective.

Basheer & Primi, *supra* note 401, at 108.

words, while weak IP rights in developing countries may not impact national innovative output detrimentally (but may, on the contrary, enhance technological capabilities through imitation), could one say the same about its net impact on global innovation? This is a more difficult question to answer. A prominent scholar notes as below:

> By weakening domestic protection, a country can stem the outflow of profit to foreign inventors without affecting the inflow of profit to its own inventors from foreign consumers. But all domestic policy makers realize this, and if they all weaken protections accordingly, the incentives to innovate may be undermined. For example, in a two-country system, if one country ceases to protect a given subject matter, the other country may reciprocate.[628]

While discussing global pharmaceutical innovation, it is important to appreciate that the current focus of leading pharmaceutical firms are developed country markets. Consequently, most R&D efforts of such firms remain focussed on 'developed' country diseases; any legal protection regime to spur higher R&D would, therefore, be framed around such diseases.[629]

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[628] *See* Scotchmer, *supra* note 215, at 13.

[629] *See* Sudip Chaudhuri et al., *Five Years into the Product Patent Regime: India's Response* (United Nations Development Program, 2010), *available at* http://apps.who.int/medicinedocs/documents/s17761en/s17761en.pdf; *see also* IMS Health, *IMS Health Reports Global Pharmaceutical Market Grew 7.0 Percent in 2006, to U.S. $643 Billion* (Mar. 20, 2007), www.imshealth.com/ims/portal/front/articleC/0,2777,6599_3665_80560241,00.html (citing a recent UNDP report studying the impact of TRIPs on the Indian pharmaceutical industry notes that Indian pharmaceutical companies earn more of their revenues from US and other developed country markets than from the domestic Indian market); *see generally* David Campell & Mandy Chui, *Pharmerging Shake-Up: New Imperatives in a Re-defined World* (IMS Health, 2007), *available at* http://www.imshealth.com/deployedfiles/imshealth/Global/Content/StaticFile/Pharma_Shake-up_Imperatives_3_10.pdf.

However, what of diseases endemic to developing countries? As noted in the introductory Chapter, the kind of drugs incentivised by high-income developed markets are drugs for diseases endemic to such countries, typically referred to Type I diseases. I discuss the broad disease categories below:[630]

### 1. Type I Diseases

Type I diseases are those that are prevalent in high-income developed countries and typically include cardiovascular disease, stroke, cancer, depression, and diabetes.[631] Some of these diseases may also be prevalent in low-income developing countries; however, the defining characteristic is a strong market demand for the treatment of such diseases in developed countries. It would appear that R&D incentives for such drugs could be sufficiently supported by the lure of high-income markets alone.[632]

### 2. Type III Diseases

Type III diseases are those that are predominantly or exclusively prevalent in developing countries, such as onchocerciasis (river blindness), leishmaniasis (kala-

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[630] *See* WORLD HEALTH ORGANIZATION, REPORT OF THE WHO COMMISSION ON MACROECONOMICS AND HEALTH REPORT OF THE COMMISSION ON MACROECONOMICS AND HEALTH, 55TH WORLD HEALTH ASSEMBLY WHO DOC. A55/5(2002) (categorising the major disease types mentioned in this thesis); *see also* JEFFREY D. SACHS, MACROECONOMICS AND HEALTH-INVESTING IN HEALTH FOR ECONOMIC DEVELOPMENT: REPORT OF THE COMMISSION ON MACROECONOMICS AND HEALTH 79 (2001), *available at* http://www.cid.harvard.edu/archive/cmh/cmhreport.pdf.

[631] *See* SACHS, *supra* note 630.

[632] *See generally* Outterson, *supra* note 604, at 160.

azar), Chagas disease, and African sleeping sickness. Global pharmaceutical firms are often accused of ignoring these diseases of the poor; such neglect is widely believed to be on account of the prospect of low returns from developing country markets, where populations are extremely poor.[633] These diseases require substantial non-market incentives, such as public funding prizes, public-private product development partnerships, advanced market commitments,[634] aspects which will be discussed in a Chapter VIII.

Depending on the disease in question and the nature of the patient population, it might also be the case that patents and data exclusivity in developing countries might offer some level of incentive for the infusion of R&D into such diseases.[635] It bears noting that while Type III diseases are predominantly endemic to developing countries, much of the health loss (as measured through DALYs) in

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[633] *See* WORLD HEALTH ORGANIZATION, INNOVATION AND PUBLIC HEALTH: REPORT OF THE COMMISSION ON INTELLECTUAL PROPERTY RIGHTS, INNOVATION AND PUBLIC HEALTH 34 (2006), *available at* http://www.who.int/intellectualproperty/documents/thereport/ENPublicHealthReport.pdf (noting that: "as is the case for diseases affecting millions of poor people in developing countries, patents are not a relevant factor or effective in stimulating R&D and bringing new products to market."); *see also* Médicins Sans Frontiéres, *Fatal Imbalance: The Crisis in Research and Development for Drugs for Neglected Diseases* (Access to Essential Medicines Campaign & Drugs for Neglected Diseases Working Group, 2001), *available at* http://www.msf.org/source/access/2001/fatal/fatalshort.pdf.

[634] *See* MICHAEL KREMER & RACHEL GLENNERSTER, STRONG MEDICINE: CREATING INCENTIVES FOR PHARMACEUTICAL RESEARCH ON NEGLECTED DISEASES 119 (2004).

[635] Only a very small portion of the disease burden in developing countries comes from these exotic tropical neglected diseases. Drugs produced for high-income markets can treat most of the global disease burden, such as the pressing need for cancer therapies in lower middle income countries, where cancer deaths outnumber AIDS deaths. The number one cause of death in lower middle income country is not a neglected tropical disease, but a familiar "rich country" killer: heart disease.

Outterson, *supra* note 554, at 321.

these countries stem from Type I and II diseases and injuries.[636]

### 3. Type II Diseases

Type II diseases share some of the characteristics of Type I and Type III diseases and are present in both developed and developing country populations. However, developing countries suffer a disproportionately large burden from such diseases. It is pertinent to note that disease categories are not static, but evolve over time. Illustratively, Tuberculosis (TB) and malaria were once Type I diseases, but are now classified as Type II by the WHO after virtual eradication of malaria in the US and Europe, and a significantly lower disease burden from TB in high-income countries. Malaria is classified as Type II, rather than Type III because it retains a small but significant financial footprint in the high-income countries to meet the needs of the military and international travelers. If multiple-drug resistant and extremely-drug resistant tuberculosis spread significantly in high-income countries, TB may regain Type I status.[637]

In so far as Type II diseases have a financially significant footprint even in the developed countries, it is likely that the innovation incentives prevalent in such developed countries may foster investments for cures to such diseases. Unfortunately, the global medical burden of diseases such as malaria and TB

[636] *See* Outterson, *supra* note 554.

[637] *See id.* at 332.

appears to have outmatched the innovation spurred by the prospect of returns from high-income country markets. These diseases may, therefore, require additional non-market incentives.

The above discussion suggests that current legal incentives such as patents and data exclusivity are not sufficient to incentivise the development of drugs for developing country or neglected diseases.[638] However, I do not intend to deliberate upon incentives for such diseases in detail. As already noted in the Introduction, this dissertation is limited to incentives for drugs to cure diseases that have a significant footprint in developed countries i.e. developed country diseases. In so far as such diseases are concerned, developed countries already have strong patent and data exclusivity regimes to help drug firms recoup their investments. Further, the last few years have seen the U.S. and the EU pressure a number of developing countries to institute strong patent and data exclusivity regimes through free trade agreements (hereinafter "FTA's").[639]

This thesis merely acknowledges this global reality (that there are a number of countries already providing for strong patent and data exclusivity protection, comprising both developed and developing countries), without investigating

[638] Type III and to some extent, Type II as well.

[639] *See generally* Charles T. Collins-Chase, *The Case against TRIPs Plus Protection in Developing Countries facing AIDS epidemic*, 29 U. PA. J. INT'L L. 763, 783 (2008); *see also* Bryan Christopher Mercurio, *TRIPs-Plus Provisions in FTA: Recent Trends, in* REGIONAL TRADE AGREEMENTS AND THE WTO LEGAL SYSTEM 215-37 (Lorand Bartels & Federico Ortino eds., 2006)*; see also* Susy Frankel, *Challenging TRIPs-Plus Agreements: The Potential Utility of Non-violation Disputes*, 12(4) J. INT'L ECO. L. 1023 (2009).

whether this number is optimal from a global innovation standpoint i.e. whether incentives in this set of developed and developing countries are sufficient for optimal global innovation or whether more countries need to institute strong regimes to protect R&D investments. This thesis asserts that in so far as a large number of countries (both developed and developing) already provide for such incentives through patents and data exclusivity, the very same countries ought to shift in favour of a more optimal investment protection regime.

In other words, the question of whether developing countries such as India ought to provide more liberal patent granting regimes[640] and data exclusivity type protection in order to further incentivise the rate of global production of cures for Type I diseases, which is already incentivised by the regimes of a large number of developed (and developing countries) is not dealt with by this thesis. As a scholar rightly notes, the minimum number of countries that ought to implement legal protection to serve the cause of global innovation is a difficult one to determine:

> One interpretation of TRIPS is that it attempts to rescue the global innovation system from the counterproductive incentive to free ride. For the most part, TRIPS obligates countries to provide certain protections, but does not proscribe stronger protections. Thus, the treaty only works in one direction, the direction of more protection.
>
> But can harmonization go too far? This is a difficult question, since it is not clear what the appropriate benchmark for global optimal protection is, and since countries with different characteristics will disagree. In general, the countries that should

[640] By *inter alia* removing patent provisions such as § 3(d) of the Indian Patents Act, 1970 which sets a high bar for pharmaceutical patent applications.

prefer stronger harmonized protection are those that are more innovative and those that are smaller.[641]

[641] *See* Scotchmer, *supra* note 215, at 13.

## CH.VIII: ALTERNATIVE INNOVATION INCENTIVES

The vast majority of drugs today cater to developed country diseases and are attributable to private firms.[642] Consequently, the investment protection regime proposed in this thesis focuses on market incentives for private firms to pursue cures for such diseases. The proposed incentives take the form of legal protection against competitors who manufacture drugs that are "similar" to that of the drug originator.

Scholars and policy makers have proposed a number of alternative incentives for innovation that eschew any form of legally sanctioned market exclusivities. In this Chapter, I consider and compare some of them with the proposed investment regime articulated in this thesis. It is pertinent to note that whilst some of these alternative mechanisms have been put into practice, others such as the Health Impact Fund (hereinafter "HIF") remain theoretical models that are yet to be implemented. Yet others, such as the public sponsorship and conduct of trials, have been proposed only as broad ideas, without any detailed discussion on how the model might work in practice. I attempt to substantiate these broad ideas by offering specific suggestions on how they might be operationalised. My hope is that the inclusion of specific suggestions will make it easier to assess the

[642] *See* Friedman, *supra* note 604.

relative strengths and weaknesses of these ideas in relation to the investment protection regime advocated in this thesis.

I argue that if our aim is to foster new cures for "developed" country diseases, none of the alternative innovation models can appropriately substitute for the investment protection regime recommended in this thesis. Nevertheless, these models could serve as supplementary innovation incentives. Further, many of these models are likely to offer better incentives for developing country diseases,[643] an aspect for which the investment protection regime in this thesis is patently ill-suited. However, a detailed discussion on this count is beyond the scope of this thesis, which deals primarily with cures for "developed" country diseases.

### A. Public Funding Model

Scholars have recommended that in view of the importance of new and affordable drugs for global health, the entire process of drug discovery and development be publicly funded. Illustratively, in the U.S. context, James Love notes: "[G]overnments could expand direct funding for drug development, either through the exi[s]ting structures such as the NIH collaborations with industry and

[643] *See* discussion in Chapter VII, *supra* text accompanying notes 633-641.

academia, or through non-profit development projects, such as those currently resourced to address treatments for neglected diseases like malaria and TB."[644]

This would enable the creation of drugs without the promise of market exclusivities and ensure that drugs are sold at competitive prices in the market, making it more affordable to the average consumer.[645] This is not to say that the process of drug innovation does not currently benefit from public funding. On the contrary, such funding is common in several countries, although it may not be comprehensive enough to fund the entire process of drug discovery and development in all cases.[646] Within the overall context of public funding for drugs,

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[644] *See* James Love, *A New Trade Framework for Global Healthcare R&D* (Workshop Hosted by the Program on Science, Technology, and Global Development, The Earth Institute at Columbia University, and the Consumer Project on Technology, Washington D.C., Dec. 4, 2003), http://keionline.org/node/943#fn_number1b (proposing and presenting an alternative to the patent system *inter alia* in the form of "direct funding of drug development" on the basis of his work in his earlier paper with Tim Hubbard); *see also* Dean Baker, *The Reform of Intellectual Property*, 32 POST-AUTISTIC ECONOMICS REVIEW 1 (Jul. 5, 2005), http://www.paecon.net/PAEReview/issue32/Baker32.htm (noting the inefficiencies plaguing the current system of patents and suggesting government funded research as an alternative to patents since it already occurs on a "massive scale"); see *also* The Free Market Drug Act, H.R. 5155, 108th Congress (2004) (seeking to create a number of public research corporations which would not only conduct basic research but also all the development required to gain approval from the FDA, although this idea never translated into law).

[645] *See* Love, *supra* note 644 (justifying the "direct funding of drug development" alternative to patent on the ground that, "[i]f exclusive marketing rights were eliminated for pharmaceutical drugs, prices would be far lower, and governments could re-direct significant resources to these types (or different types) of non-profit drug or vaccine development entities.").

[646] NIH spends more than U.S. $31.2 billion annually in medical research (May SW 'for the people of America/Americans) (last updated Mar. 9, 2011). National Institutes of Health, *About NIH: NIH Budget*, http://www.nih.gov/about/budget.htm#note (last visited Sept. 30, 2011); *see* Hamilton Moses III *et al.*, *Financial Anatomy of Biomedical Research*, 294 J. AM. MED. ASS'N. 1333-42 (2005) (indicating that the U.S. appears to be the leading governmental contributor to global public health expenditure); *see also* ANGELA RITZVERT ET AL., UNITED STATES CONGRESS JOINT ECONOMIC COMMITTEE, THE BENEFITS OF MEDICAL RESEARCH AND THE ROLE OF THE NIH (May 17, 2000); *see also* EUROPEAN SCIENCE FOUNDATION, EMRC WHITE PAPER: PRESENT STATUS AND FUTURE STRATEGY FOR MEDICAL RESEARCH IN EUROPE 16-19 (2007).

many scholars have begun recommending that clinical trials be publicly funded owing to the potential for bias arising from corporate sponsorship.

Critics have severely excoriated this framework of interest-driven trials on several grounds, some of which are highlighted below:[647]

i) Corporate financing of clinical research often tends to bias results, yielding positive results far more often than would have been the case, had the studies been funded or conducted by a neutral entity with no stake in the trial.[648]

ii) The likelihood of methodological biases stemming from the enrolment of relatively healthy patients, insufficient dosage of the comparator drug, inadequate sample size and inappropriate length of patient follow-up.

iii) The comparison of novel treatments against a placebo than against existing drugs, which are known to be effective.[649]

iv) The likelihood of bias in the reporting of industry sponsored clinical trials. Illustratively, some firms have been accused of withholding the publication of unfavourable results.[650]

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[647] *See* Sameer S. Chopra, *Industry Funding of Clinical Trials: Benefit or Bias?*, 290(1) J. AM. MED. Ass'N. 113, 113-114 (2003), *available at* http://jama.ama-assn.org/content/290/1/113.full.

[648] *See* Dean Baker, *The Benefits and Savings from Publicly Funded Clinical Trials of Prescription Drugs*, 38(4) INT'L. J. HEALTH SERV. 731, 733 (2008).

[649] *See* B. Djulbegovic et al., *The Uncertainty Principle and Industry-sponsored Research*, 356 LANCET 635 (2000).

For all the above reasons, scholars recommend alternative mechanisms of trial sponsorship, design and conduct.[651] In a persuasive paper, Tracy Lewis et al. propose that clinical trials be undertaken by a neutral public funded body with no links to the pharmaceutical industry or any other person with a direct stake in the drug under testing.[652] However, they merely recommended this core idea,[653] without offering any details on how the model could be operationalised. I, therefore, begin by making some comprehensive suggestions in this direction before evaluating the merits of such a regime.

As a common baseline, I recommend that clinical trials be administered and funded through a neutral third party organization with no vested interest in the outcome of the trial.[654] Member states would have to contribute funding for such an

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[650] In one example, a pharmaceutical company delayed for 7 years the publication of a study concluding that its widely prescribed preparation of levothyroxine was no more effective than less expensive generic formulations. Thomas Bodenheimer, *Conflict of Interest in Clinical Drug Trials: A Risk Factor for Scientific Misconduct* (2000), http://www.hhs.gov/ohrp/archive/coi/bodenheimer.htm; *see also* Chopra, *supra* note 647, at 607.

[651] *See* Thomas Bodenheimer, *Uneasy Alliance-Clinical Investigators and the Pharmaceutical Industry*, 342 N. ENG. J. MED. 1539, 1543 (2000) (recommending that investigators independently control the design, implementation, data analysis and publication, even if they are funded by drug companies).

[652] *See* Tracy R. Lewis et al., *The Case for Public Funding and Public Oversight of Clinical Trials*, 4(1) ECONOMISTS VOICE (2007); *see also* Jayadev & Stiglitz, *supra* note 307 ("[c]ost increases in clinical trials, especially during stage (III) trials, have made the overall production cost of a new chemical entity prohibitively expensive. One proposal to achieve these ends that appears very appealing is the idea to publicly fund clinical trials in pharmaceuticals.").

[653] *See* Lewis, *supra* note 639; *see also* Jayadev & Stiglitz, *supra* note 307; *see also* John J. McNeil et al., *Public Funding of Large-scale Clinical Trials in Australia*, 179(10) MED. J. AUSTRALIA 519 (2003).

[654] It is pertinent to note in this regard that global pharmaceutical firms have begun to outsource clinical trials to countries such as India and there is a growing pool of talented third party experts adept at the conceptualisation and management of trials. NASSCOM Newsline, *Emerging Vertical-*

organisation, in accordance with their Gross Domestic Product (hereinafter "GDP")[655] or Gross National Product (hereinafter "GNP").[656] One might draw a parallel in this regard from the proposed Global R&D treaty, which mandates an equitable sharing of financial burden, depending upon the respective GDP of member states.[657] This treaty is discussed in greater detail later in this Chapter.

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*Clinical Research Outsourcing*, http://blog.nasscom.in/nasscomnewsline/wp content/uploads/pdf_/eye_on_the_Industry_may09.pdf (last visited: Oct. 3, 2012); *see also* Roger Crossley, *The Quiet Revolution: Outsourcing in Pharma*, 9(16) DRUG DISCOVERY TODAY 694 (2004); *see also* James Cekola, *Outsourcing Drug Investigations to India: A Comment on U.S., Indian, and International Regulation of Clinical Trials in Cross-Border Pharmaceutical Research*, 28 NW. J. INT'L L. & BUS. 125 (2007-2008); *see also* Carolyne R. Hathaway et al., *Looking Abroad: Clinical Drug Trials*, 63 FOOD & DRUG L. J. 673 (2008); *see also* Fernando Santiago Rodriguez & Gabriela Dutrenitc, *Determinants of PRO-industry Interactions in Pharmaceutical R&D: The Case of Mexico*, 22 (Globelics 2010, 8th International Conference, University of Malaya, Kuala Lumpur, Malaysia, Nov., 2010), *available at* http://umconference.um.edu.my/upload/431/papers/212%20FernandoSantiagoRodriguez_GabrielaDutrenit.pdf; *see also* Madhur Singh, *Should Clinical Trials be Outsourced*http://www.time.com/time/health/article/0,8599,1830334,00.html (last visited Sept. 30, 2011) (noting that there are currently some 400 clinical trials underway in India, where the business is expected to grow to US $1 billion to US $1.5 billion by 2010).

[655] Simply put, GDP is the value of all final goods and services produced in a country in one year. GDP can be measured by adding up all of an economy's incomes, wages, interest, profits, and rents or expenditures consumption, investment, government purchases, and net exports (exports minus imports). Both results should be the same, because one person's expenditure is always another person's income, so the sum of all incomes must equal the sum of all expenditures. WORLD BANK, *Beyond Economic Growth: Student Book-Glossary*, http://www.worldbank.org/depweb/english/beyond/global/glossary.html#34 (last visited Sept. 30, 2011).

[656] GNP is the value of all final goods and services produced in a country in one year (gross domestic product) plus income that residents have received from abroad, minus income claimed by non-residents. GNP may be much less than GDP if much of the income from a country's production flows to foreign persons or firms, but if the people or firms of a country hold large amounts of the stocks and bonds of firms or governments of other countries, and receive income from them, GNP may be greater than GDP. For most countries, however, these statistical indicators differ insignificantly. *Id.*; *see also* G.A. Res. 247[B], U.N. GAOR, 36th Sess. (1985); *see also* UNITED NATIONS, *Briefing on Methodology the Scale of Assessment*, *available at* http://www.un.org/en/ga/fifth/Presentations/64th%20Session/scale-method.pps (last visited Sept. 30, 2011) (noting that contributions to the expenditures of the United Nations (UN) are apportioned among the member states in accordance with their capacity to pay (determined on the basis of their Gross National Product)).

[657] *See* CPTech*, Proposal for Treaty on Medical Research and Development* (Feb., 2005), http://www.cptech.org/workingdrafts/rndtreaty.html#Status; *see also* CPTech, *Who Pays What?* (Working Draft, 2002), www.cptech.org/workingdrafts/whopayswhat.xls.

For the purposes of this thesis, let us label this body as the International Centre for Drug Development (hereinafter "ICDD"), brought into existence through an international treaty. This body could be made to work in the following ways:

1. By merely funding the trials, the execution and administration of which continue to vest with the pharmaceutical firm credited with the IND approval for a certain "lead."

2. By administering the conduct of the trials by itself or with the help of a third party organisation that has no links with the originator of the lead molecule being developed. For this to work, the originator must, after it procures IND approval, co-operate with the ICDD or the chosen third party supervisor.

The latter option is more attractive since it increases the objectivity associated with trials, and, in turn, could be made to work as below:

1. Only applicants, who file INDA's or its equivalent (CTA in the EU) and procure regulatory approvals to conduct trials, are entitled to apply for sponsorship under this scheme.[658] Given that very few regulatory agencies

[658] As noted in Chapter I, an IND is an application seeking permission from the FDA to test a drug candidate in humans. This application contains laboratory-tested and other pre-clinical evidence to demonstrate that the drug is sufficiently effective and safe to be tested in humans. Once the IND is submitted, the sponsor must wait 30 calendar days before initiating any clinical trials. During this time, the FDA has an opportunity to review the IND. U.S. FDA, *Investigational New Drug (IND)*

such as the U.S. FDA and the EMEA have a reputation for stringent review of drug applications, the model should, at this stage, take account of only IND-type approvals from such reputed regulatory authorities.[659]

2. Once an INDA is submitted, the drug applicant can opt to have its clinical trials sponsored and administered by the ICDD. Alternatively, it could conduct the trials itself and opt to avail of "data exclusivity" protection under existing incentive regimes.[660] However, if the proposed regime is to work well, countries must gradually abolish their data exclusivity regimes, forcing firms to adopt this new model of public funding and sponsorship.

3. Assuming that the applicant opts for ICDD sponsorship, the ICDD takes over the process of supervising the trials. It has the flexibility to engage any third party organisation for helping it with this task.

4. Assuming the drug is approved, there are no legal exclusivities and both the IND applicant and any interested third parties are free to market and

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*Application*, http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm (last visited Sept. 30, 2011); *see also* Saudi Food and Drug Authority, *Guidelines for Investigational New Drugs (IND) Requirements*, 6 (Aug., 2009), *available at* http://www.sfda.gov.sa/NR/rdonlyres/425A5ACA-E37B-4F20-AF7A-88C64D1DD671/0/GuidelinesforInvestigationalNewDrugsINDRequirements.pdf.

[659] *See* John Abraham & Courtney Davis, *A Comparative Analysis of Drug Safety Withdrawals in the U.K. and the U.S. (1971-1992): Implications for Current Regulatory Thinking and Policy,* 61 SOCIAL SCI. & MED. 881 (2005) (emphasising the stringent review standards of the FDA). *Cf.* DANIEL CARPENTER, REPUTATION AND POWER: ORGANIZATIONAL IMAGE AND PHARMACEUTICAL REGULATION AT THE FDA (2010) (arguing that the FDA's reputation and power have declined in the past decade owing to mishandling of a number of safety issues).

[660] The U.S., EU and Japan are the three main jurisdictions, which grant data exclusivity protection for various periods depending upon the kinds of drugs seeking approval. Charles Clift, *The Value of Patent Term Extensions to the Pharmaceutical Industry in the USA*, 5 J. GEN. MED. 201-208 (2008)

sell the drug. However, the third party applicant would have to comply with all formalities that a regular generic applicant is subject to i.e. demonstrate that the active ingredient in the application is bio-equivalent to the originator molecule approved by the FDA.[661]

The above framework could serve as a template for a more nuanced regime, premised on public sponsorship and supervision of trials. As with the investment protection regime advocated in this thesis, an international model is preferable to a purely national one.

It is pertinent to note in this connection that leading drug regulatory agencies and pharmaceutical industry associations came together in 1996 as the International Conference on Harmonization (hereinafter "ICH"), to harmonize regulatory standards and reduce the burden on multinational pharmaceutical firms.[662] While the ICH guidelines are primarily applicable to three major drug regulatory jurisdictions, namely the U.S., EU and Japan, the ICH has been constantly

[661] However, in so far as biologics are concerned, the drug molecule in question must be shown to be "highly similar" to the referenced product in the US, and "similar" to the referenced product in the EU. Art. 10.4, 42 U.S.C. §262(k)(2)(A)(i)(I); *see also* Council Directive 27/EC (2004).

[662] It is composed of both regulators and industry representatives from the US, EU and Japan. The purpose of ICH is "to achieve greater harmonization in the interpretation and application of technical guidelines and requirements for product registration in order to reduce or obviate the need to duplicate the testing carried out during the research and development of new medicines." International Conference on Harmonization*, History and Future of the ICH*, *available at* http://www.ich.org/about/history.html (last visited Sept. 30, 2011).

expanding its international reach by entering into strategic alliances.[663] The above harmonization efforts bear the promise of a meaningful international drug regulatory regime in the years to come.[664]

### 1. Drawbacks of the Model

As with any regime dependent on public funding, the main criticism against such a model is that relies extensively on the political will of governments, both at the national and international levels.

Second, even assuming that states were to fund the entire drug discovery and development process, one is not certain if the private sector would expend their time and effort to create drugs using such public funding, when the final drug is open to manufacture by their competitors. In other words, drug originators do not gain any additional financial benefit from creating the drug. Therefore, one may argue that an IND applicant is more likely to opt for existing exclusivity regimes such as patents and data protection to protect their investments rather than opting

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[663] Illustratively, in 1999, the ICH created the Global Cooperation Group to communicate with regional harmonization groups outside the ICH. Additionally, the WHO and Health Canada, the central Canadian public health agency, are official observers to the ICH. International Conference on Harmonization*, ICH Global Cooperation Group, available at* http://www.ich.org/meetings/gcg-reports.html (last visited Sept. 30, 2011). (inviting participation from the Asia-Pacific Economic Cooperation (APEC), the Association of Southeast Asian Nations (ASEAN), the Gulf Cooperation Countries (GCC), the Pan American Network on Drug Regulatory Harmonization (PANDRH), and the Southern African Development Community (SADC).)

[664] *See* Nathan Cortez, *International Health Care Convergence: The Benefits and Burdens of Market-Driven Standardization*, 26(3) WIS. INT'L. L. J. 647 (2008) (elaborating discussion in this regard).

for the public funded model. This could be rectified by offering a monetary prize upon the successful creation of a drug, an aspect dealt with later in this Chapter.

It is also doubtful if an IND applicant would spend time and resources aiding the ICDD with its trials, when the benefits are likely to flow to market competitors as well. Such co-operation would be necessary in many cases, given that the IND applicant may have more intimate knowledge about the lead molecule. If the drug may need to be modified in terms of its formulation, dosage, etc., the IND applicant is likely to be better placed to undertake such modifications.[665] However, without the prospect of additional financial returns, one may argue that an IND applicant is not likely to expend valuable time by co-operating with the ICDD.

Thirdly, when viewed through the lens of public choice theory, any model that relies excessively on public funding is prone to issues such as regulatory capture. Public choice theory works on the assumption that voters, politicians are bureaucrats are self-interested actors that seek to maximise their potential gains as opposed to acting purely in the interests of the public.[666] According to Gordon Tullock,

> … Just as a businessperson designs, let us say, the latest automobile so as to attract customers, the politician selects policies with the idea that

[665] *See* Saudi Food and Drug Authority, *supra* note 658.

[666] *See* Gordon Tullock, *Public choice*, *in* THE NEW PALGRAVE DICTIONARY OF ECONOMICS (Steven N. Durlauf &Lawrence E. Blume eds., 2008).

> the customer, who is the voter, will reward the politician in the next election […] Politicians and businesspeople will sometimes pay a price (lost constituent support) in order to do what they think is good, but on the whole they can be expected to act in such a way as to maximize their own well-being in terms of re-election prospects.[667]

Regulatory capture lies at the very heart' of public choice theory and suggests that firms exert significant influence on government decision-making[668]and that regulation is often designed in response to the demands of individual interest groups that compete among themselves to maximize the interests of their members.[669]

Fagin cites the example of government funding of science and argues that since politicians are motivated to conform their behaviour and policies to that which would most favour their re-election efforts, they are likely to use federal funds earmarked for science in a manner that concentrates "the benefits on desired recipients, typically in their home state, and by diffusing the costs over a large taxpayer base, legislators pursue their own self-interest (and, in all

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[667] GORDON TULLOCK, *The theory of public choice*, *in* GOVERNMENT FAILURE 1, 6 (2002).

[668] *See* Jeffrey T. Macher, John W. Mayo, and Mirjam Schiffer, *The Influence of Firms on Government*, 11(1) B.E. J. ECON. ANALYSIS & POL'Y (2011), at 22 ("That firms seek to influence governmental decision-making is incontrovertible."). See also George J. Stigler, *The Theory of Economic Regulation*, 2 BELL J. ECON. MGMT. SCI. 3,3 (1971).

[669] *See* Richard A. Posner, *Theories of Economic Regulation*, 5(2) 2 BELL J. ECON. MGMT. SCI. 335, 335-336 (1974); *see also* J.J. Laffront & Jean Tirole, T*he Politics of Government Decision-Making: A Theory of Regulatory Capture*, 106 (4) Q. J. ECON. 1089-1127 (1991) and Lawrence G. Baxter, *"Capture" in Financial Regulation*: *can we channel it toward the common good?*, 21 CORNELL J.L. & PUB. POL'Y 175, 175 (2011).

fairness , those of at least some voters), at the expense of overall social welfare."[670]

Similarly, the FDA has been accused of regulatory capture by leading pharmaceutical companies in the US.[671] The close nexus between the regulator and the industry is attributed partly to the 'revolving door' – officials at the agency often start their careers in the industry and after spending some time at the regulatory agency are employed back in the industry.[672]

Considering the above, it is likely that any regime dependent on public funding is prone to some form of regulatory capture. However, one might deploy a number of measures to reduce the prospects of such capture. These include empowerment of public interest groups, ensuring greater participation in the regulatory process or 'tripartism'[673], rotating regulatory officials for limiting "transference" to reduce the proximity of the same regulators to the industry they regulate for a prolonged period[674] and tackling the 'revolving door' phenomenon by having "formal ethical rules barring direct engagement on matters where

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[670] Barry S. Fagin, *The application of public choice theory to science and engineering policy*, Proceedings of the 1993 International Conference of the American Society for Engineering Education, Champaign-Urbana, Illinois (1993) (citing JOSEPH MARTINO, SCIENCE FUNDING (1992)).

[671] *See* John Abraham, *The pharmaceutical industry as a political player*, 360 LANCET 1498 (2002); Ray Moynihan, *Alosetron: a case study in regulatory capture, or a victory for patients' rights?*, 325 BRIT. MED. J. 592 (2002).

[672] *See* Abraham, *supra* note 671, at 1498.

[673] *See* Baxter, *supra* note 669, at 191 (citing Ian Ayres & John Braithwhite, *Tripartism:Regulatory Capture and Empowerment*, 16 LAW & SOC. INQUIRY 435, 439 (1991)).

[674] *See* Baxter, *supra* note 669, at 196.

regulators have already been on the industry side"[675] or by "outright exclusion of the employee from subsequent agency access", or by "requiring post-employment statements to be made publicly available."[676]

To conclude, any model based on public funding alone is likely to face difficulties. Such a model may require to be supplemented with other incentives such as prizes in order to work more optimally.

### B. The Prize Regime

The concept of prizes predates even the patent system and has been advocated by many scholars as a more optimal alternative incentive.[677] Distilled to its bare essence, the concept of a prize is as follows: a sponsor announces a reward for a specific kind of innovation and makes good the promised reward to any person/entity that comes up with the relevant innovation. In the context of pharmaceutical innovation, the Health Impact Fund (hereinafter "HIF") is a good example of a prize, where drug innovators are rewarded based on the therapeutic

[675] *Id.,* at 197.

[676] *Id.*

[677] Napolean was keen on finding an effective way to feed his troops in areas where food could not otherwise be procured locally. In 1809, Nicolas François Appert won the prize for his solution, which involved heating, boiling and then sealing the food to be preserved in airtight glass jars. The basic principles of canning have not changed much since Nicolas Appert's methods were published. James Love & Tim Hubbard, *Prizes for Innovation in New Medicines and Vaccines*, 22 (2008), *available at* http://policydialogue.org/files/events/Love_Hubbard_Prizes_for_Innovation_in_Medicines_and_Vaccines.pdf.

value of their products through a government sponsored fund.[678] This model will be discussed at length later in this Chapter.

Prizes are not a new concept; notable historical examples include a prize instituted by Napoleon in 1795 for an effective method for preserving food[679] and an award of £1000 by the British House of Commons for a new method of draining farmland to make it better suited to raising crops or supporting livestock.[680] As can be seen from the above examples, a prize could be *ex ante*, in that it specifies a desired outcome and a reward for obtaining it, or *ex post,* where a certain achievement is rewarded after the fact. The Napoleon "food preservation" prize is an example of the former and the Elkington prize an example of the latter.

In its application to drug discovery and development, prizes have not had much success. However, it has been proposed by several scholars[681] as an effective incentive to foster the creation of drugs for developing country diseases (Type III

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[678] *See* Hollis, *supra* note 75.

[679] *See* Love & Hubbard, *supra* note 677.

[680] In 1764, Joseph Elkington, an illiterate but very bright Warwickshire farmer, first discovered, and later refined, a new and effective system of draining farmland to make it better suited to raising corps or supporting livestock. Elkington sold his services to landowners seeking more effective systems of drainage. While news of Elkington's success spread, much remained unknown regarding his techniques; in 1795, the British House of Commons authorized 1,000 pounds to offer as an inducement for Mr. Joseph Elikington to disclose and disseminate more widely his mode of draining. Elikington accepted the reward and disclosed his method to the public. *Id.*

[681] *See* Fisher & Syed, *supra* note 443, at 24; *see also* Joseph Stiglitz, *Give Prizes not Patents*, NEW SCIENTIST 21 (Sept. 16, 2006).

diseases).[682] They contend that prizes are likely to provide strong incentives for research, whilst avoiding the inefficiencies inherent in legal monopolies.[683]

In 2001, Eli Lilly, a global pharmaceutical firm created "InnoCentive," an entity to administer a series of commercially-sponsored prizes to solve specific problems in the area of life sciences. Since then, a number of philanthropic organizations have sponsored medical innovation prizes, including but not limited to the X-Prize Foundation, the Prize4Life Foundation, and the Gotham Prize.[684] A U.S. bill titled "Medical Innovation Prize Fund (MIPF) Act, 2005" proposed a prize driven innovation incentive, but was never passed into law.[685] Its successor, the "Medical Innovation Prize Fund (MIPF) Act, 2007" met with a similar fate and has now been replaced by the "Medical Innovation Prize Fund (MIPF) Act, 2011".[686] These Bills aim at providing incentives for investment in therapeutically significant medicines, particularly neglected diseases and orphan diseases and in ensuring affordable access to such medicines.[687] The core principles underlying these Bills

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[682] *See* Fisher & Syed, *supra* note 369.

[683] *See* Stiglitz, *supra* note 681.

[684] *See* Love & Hubbard, *supra* note 677, at 11; *see also Selected Innovation Prizes and Reward Programs* 7-9 (KEI Research Note No. 1, 2008), http://www.keionline.org/misc-docs/research_notes/kei_rn_2008_1.pdf (enlisting comprehensive list of prizes).

[685] *See Medical Innovation Prize Act of 2005*, *available at* http://www.govtrack.us/congress/bill.xpd? bill=h109-417, (last visited Sept. 30, 2011).

[686] *See* Library of Congress*, Bill Summary and Statuts of 112th Congress (2011-12) S. 1137,* a http://thomas.loc.gov/cgi-bin/bdquery/z?d112:s.1137_(last visited Sept. 30, 2011) (stating that the bill was read twice and referred to the Committee on Health, Education, Labour, and Pensions).

[687] In the words of Representative Bernard Sanders, who is credited with initiating these bills: [r]ather than rely[ing] on high drug prices as the incentive for R&D, the bill would directly reward developers of medicines, on the basis of the incremental therapeutic benefit to consumers, through a

are drawn from a global R&D treaty model proposed by James Love and Tim Hubbard, a model discussed in a later section of this Chapter.[688]

A prize regime is not necessarily incompatible with a patent regime. On the contrary, it is capable of co-existence, as will be evident from the HIF model (discussed later in this Chapter), where the recipient of a prize fund commits only to selling the final product at low prices, but is not prevented from using her patent exclusivity to keep competitors out of the market. However, some prizes expressly mandate "patent buy-outs," a mechanism by which the patent is purchased, typically by governments that estimate the private value of a patent through an auction.[689] Illustratively, consider Louis Jacques Mande Daguerre's patented invention of photography in the nineteenth century.[690] Considering the importance of the invention, the French Government purchased it and placed it in the public

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new Medical Innovation Prize Fund. Prices for prescription drugs to consumers would be at low generic prices immediately upon entry to the market. By breaking the link between drug prices and R&D, it would provide more equitable access to medicine, end rationing and restrictive formularies, and manage overall R&D incentives through a separate mechanism that can be increased or decreased, depending on society's willingness to pay for medical R&D. Marlynn Wei, *Should Prizes Replace Patents?: A Critique of the Medical Innovation Prize Act*, *2005,* 13 B. U. J. SCI. & TECH. L. 25, 28 (2007); *see also* Office of Legislative Policy and Analysis, *Medical Innovation Prize Act of 2005,* http://olpa.od.nih.gov/legislation/109/pendinglegislation/medicalinnovation.asp (last visited Sept. 30, 2011).

688 *See* Love & Hubbard, *supra* note 677, at 11.

689 *See* Michael Kremer, *Patent Buy-outs: A Mechanism for Encouraging Innovation*, (NBER Working Paper No. 6304, December, 1997) *available at* http://www.nber.org/papers/w6304.pdf?new_window=1.

690 While Daguerre is generally hailed as the father of modern photography, historians claim that it was his collaborator and partner, Niépce who is to be credited as the inventor of photography. Niépce's "heliographic" process, developed prior to his collaboration with Daguerre, was the first successful example of what we now call photography, an image created on a light-sensitive surface, by the action of light. *See* Jessica Gorman, *Photography at a Crossroads: In this Digital Era, the Future of Historical Photos is at Stake*, 162(21) SCIENCE NEWS 331 (Nov., 2002).

domain.[691] As a result, it was adopted rapidly and within months, a multitude of improvements were made to the initial patented process.[692] Abramowicz recommends a system where prizes are coupled with patent buyouts. He argues that such a system would lead to considerable savings, since there would be no need for a prize recipient to enforce its patent through expensive litigation.[693]

The prize system has not been without its fair share of criticisms.[694] Firstly, prize system fosters inefficient "rent seeking," in that companies would try and influence the government to alter the ways in which the prizes are calculated and allocated.[695]

Secondly, there is considerable distrust of governments in making good their promises to award prizes. As a result, governments may need to increase the magnitude of the promised prize to offset any hesitation felt by pharmaceutical companies in spending huge sums of money on R&D on this account.[696]

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[691] The French government agreed to award Daguerre a yearly stipend of 6,000 Francs for the rest of his life. L. J. M. DAGUERRE, HISTORY AND PRACTICE OF PHOTOGENIC DRAWING 2 (1839).

[692] *See* M. SUSAN BARGER & WILLIAM B. WHITE, THE DAGUERREOTYPE 34 (1991).

[693] *See* Michael Abramowicz, *Perfecting Patent Prizes* 66 (George Mason Law & Economics Research Paper No. 01-29, 2001), http://papers.ssrn.com/sol3/papers.cfm?abstract_id=292079.

[694] A number of criticisms are aimed at government sponsored prizes, and may not therefore apply to prizes administered by private agencies.

[695] *See* Fisher & Syed, *supra* note 681, at 12-13.

[696] *See id.* at 13-14.

Thirdly, even if prizes are successful in stimulating inventions, they may fail to encourage entrepreneurs to invest in the commercial development of such inventions.[697] However, this problem could be tackled by providing rewards for both the "invention" as well as the final "product" which is developed and marketed.

Lastly, most prizes are premised on clearly defined innovation goals, which are stipulated at the outset.[698] To this extent, prizes are not oriented towards fostering more open-ended innovations (without reference to specific problems), in the way that patents do.[699] This problem can however be tackled through a broad "blue-sky" prize model. Unlike the "targeted" prize model, which specifies the problem to be solved and in some cases, even the broad range of potential solutions, blue-sky prizes offer contestants the freedom to choose the problems that they wish to study and locate solutions for. To this extent, blue-sky prizes are problem agnostic and any contestant who produces the most valuable research receives a reward. The key challenge for prize designers is in determining the precise model to implement along the continuum between targeted and blue-sky

[697] Under the patent system however, since the patent right can be enforced to prevent rivals from entering the market with a similar product for a significant period of time, the patentee has sufficient motivation to make the expenditure necessary to commercialize the product and maximize the value of the patent before it expires. Abramowicz, *supra* note 669, at 41-43.

[698] *See* Fisher & Syed, *supra* note 681, at 20-23; *see also* Marlynn Wei, *supra* note 687, at 4.

[699] *See* Fisher & Syed, *supra* note 681, at 20-23.

prizes.[700] The HIF is a good illustration of a blue-sky prize model aimed at fostering pharmaceutical innovation.

### C. The Health Impact Fund

The Health Impact Fund (hereinafter "HIF") was proposed by two reputed scholars as a mechanism to provide an incentive for the creation of new drugs with a significant health impact. It is a specific kind of "prize," wherein creators of new drugs are rewarded out of a global fund, the reward being proportionate to the health impact of the drug. More specifically, the HIF would pay out over a pre-defined number of years, for e.g., a new pharmaceutical product might earn payments from the HIF every year for its first 10 years of use.[701] In this respect, the HIF differs from a patent buy-out, in that the drug originator continues to own the intellectual property, but agrees to desist from charging a monopoly price. Instead, the drugs have to be sold globally at no more than the lowest feasible cost of production and distribution.[702]

The originators of the HIF model steer clear of recommending it as a

[700] *See* STEPHEN MAURER, WHO COMMISSION ON INTELLECTUAL PROPERTY RIGHTS, INNOVATION AND PUBLIC HEALTH, THE RIGHT TOOL(S): DESIGNING COST-EFFECTIVE STRATEGIES FOR NEGLECTED DISEASE RESEARCH 79 (Mar. 29, 2005), *available at* http://www.who.int/intellectualproperty/studies/research_development/en/index.html.

[701] *See* Aidan Hollis, *The Health Impact Fund: A Useful Supplement to the Patent System?*, 1(2) PUB. HEALTH ETHICS 124, 127 (2008).

[702] *See* Health Impact Fund, *A Proposal of Incentives for Global Health*, http://www.yale.edu/macmillan/igh/pilot.html (last visited Sept. 30, 2011).

substitute for the patent system. Rather, they advocate this as a supplement to the patent system. Given that the HIF system is optional, firms are likely to elect it only when they expect greater returns from the HIF fund when compared with an unconstrained use of patent exclusivity. This considerably mitigates the risks firms face in terms of the limited HIF budget and the uncertainty associated with the quantum of the HIF funds that they compete for. Should the payment per QALY drop too low, it is likely that firms will prefer patents to the HIF system. In turn, this drop out of firms from the HIF system increases the payment per QALY for those firms which opt to remain within the system.[703]

Pogge and Hollis had initially restricted eligibility to only patented drugs.[704] However, pursuant to a scathing critique,[705] this pre-requisite was dropped and it was acknowledged that a mere marketing approval from the leading regulatory authorities (for instance the FDA) would suffice.[706]

In order to work effectively, the HIF requires a massive infusion of funds. The authors of the model recommend an annual funding of least U.S. $2 billion –

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[703] *See* Hollis, *supra* note 701, at 129.

[704] *See id.* at 14.

[705] *See* Talha Syed, *Should a Prize System for Pharmaceuticals Require Patent Protection for Eligibility* (IGH Discussion Paper No. 2, Jun., 2009), *available at* http://www.yale.edu/macmillan/igh/files/DP2_Syed.pdf.

[706] *See* Aidan Hollis & Thomas Pogge, *The Health Impact Fund: Making New Medicines Accessible to All- Supplements and Corrections* (Nov., 2009), http://www.yale.edu/macmillan/igh/files/HIF_supplementsNov09.pdf.

U.S. $10 billion.[707] In order to make the fund credible enough for firms to participate, the authors propose that countries commit substantial funding far into the future, at least for a minimum of 12 years.[708] Apart from an international treaty that obligates countries to pay moneys into a common fund, commensurate with their respective per capita income,[709] funding could also flow from private philanthropic organizations.[710] Illustratively, charitable organizations such as the Gates Foundation[711] have been funding drug research in relation to several diseases, most notably neglected diseases, and it is conceivable that such contributors could step in to help the HIF too.[712] Given that the operation of the HIF model is likely to reduce drug prices (since a drug originator who avails of the HIF reward has to mandatorily sell at a price close to the manufacturing cost), and the corresponding burden on governments who pay for such drugs as part of their public health programmes, governments too could be persuaded to contribute to the fund.

Any new drug originator is entitled to register with the HIF and stake a claim for a portion of the fund. Such registration would require the drug firm to sell its

[707] *See* Hollis, *supra* note 701, at 129.

[708] *See* Hollis & Pogge, *supra* note 706, at 10.

[709] *See* Hollis, *supra* note 701, at 130.

[710] *See id*.

[711] *See* Bill and Melinda Gates Foundation, *Global Health Program*, http://www.gatesfoundation.org/global-health/Pages/overview.aspx (last visited Sept. 30, 2011).

[712] *See* Hollis, *supra* note 701, at 130

product worldwide at an administered price near the average cost of production and distribution. The administered price will also be listed on the official HIF website, such that wholesale buyers are aware of it. Thus, the registrant retains exclusivity in the product, but foregoes the monopoly price in return for payments from the HIF. In exchange, the firm would receive a stream of payments from the HIF based on the relative incremental global health impact of its drug.[713]

The HIF regime requires an administrative branch to annually estimate the health impact of each product so that drugs are rewarded commensurate with their impact. The originators of the model, Pogge and Hollis recommend the establishment of an Independent Assessment Committee (hereinafter "IAC") for this purpose, to determine health impact in accordance with existing quality measures such as QALY, as also to examine evidence presented by the drug applicant, governments, and other sources, including its own investigations. Importantly, they recommend the institution of a comprehensive information gathering and assessment system. Further, they note that one could use epidemiological studies to refine these estimates of health impact after the drug had been in use for some time.[714] The authors acknowledge that, for the model to

[713] *See* Hollis & Pogge, *supra* note 706, at 1.

[714] *See* Aidan Hollis, *A Comprehensive Advance Market Commitment: A Useful Supplement to the Patent System?* 13 (Nov., 2007), http://www.yale.edu/macmillan/igh/files/ PHE_Hollis_CAMC.pdf.

work well, health impact data would be needed to be updated on a regular basis, taking into account physician survey data about the actual use of the drugs.[715]

The key advantage of the HIF model is that it fosters the creation of low priced drugs with significant global health impact. As noted earlier, global pharmaceutical firms do not devote sufficient resources to Type III diseases or diseases of the poor.[716] Given the reality that developed country markets are far more profitable than developing country markets, the patent system would continue skewing research in favour of rich (developed country) drugs. The HIF model has the potential to redress this incentive malaise to some extent. In fact, advocates of the HIF model suggest that the fund ought to direct rewards toward Type III diseases— diseases that are prevalent mainly in low and medium income countries, and for which no viable market exists in high-income countries—since those are the ones for which patent exclusivity creates the weakest incentives for research.[717]

The HIF system is advantageous over other regimes that have been proposed for incentivising cures for neglected diseases, such as advance market

[715] This could be done by an independent global health consultancy firm such as IMS Health based on patient usage data and evidence from practical trials and data from post approval clinical trials. Amitava Banerjee et al*., The Health Impact Fund: Incentives for Improving Access to Medicines*, 375 LANCET 166, 168 (2010).

[716] *See id.* at 166.

[717] Examples include diseases such as lower respiratory tract infections and Burkitt's lymphoma. *Id.* at 166-168; *see also* Thomas Pogge, *Access to Medicines,* 1(2) PUB. HEALTH ETHICS 73, 76-77 (2008).

commitments (hereinafter "AMC"). Firstly, unlike an AMC, it is not drug-specific and, therefore, will not be susceptible to pressure from any particular pharmaceutical lobby group.[718]

The HIF model is also likely to offer better incentives than the patent system in relation to the search for "new uses'' of known drugs. It is pertinent to note that new uses of known substances are excluded from patentability in some countries.[719] Even in those countries where it is patentable, it is difficult to enforce such a patent, since a generic manufacturer could claim that it is manufacturing and selling the drug for the old use. Under the HIF approach however, a firm need not rely on patent exclusivities to make its profits. Rather, it could claim a reward from the HIF fund commensurate with the health impact of its newly discovered use for the drug in question. Another advantage of the HIF model is in terms of its potential to reduce the menace of counterfeit drugs. With the genuine drug available at prices very close to the marginal cost of production, there is little to be gained from producing and selling fakes.[720]

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[718] Thomas Alured Faunce & Hitoshi Nasu, *Three Proposals for Rewarding Novel Health Technologies Benefitting People Living in Poverty*: *A Comparative Analysis of Prize Funds, Health Impact Funds and Cost-Effectiveness/Competitive Tender Treaty*, 1(2) PUB. HEALTH ETHICS 146 (2008).

[719] For a discussion on new uses, see Chapter II, *supra* text accompanying notes 164-165.

[720] *See* Thomas Pogge, *The Health Impact Fund: Better Pharmaceutical Innovations at Much Lower Prices, in* INCENTIVES FOR GLOBAL HEALTH: PATENT LAW AND ACCESS TO ESSENTIAL MEDICINES (Thomas Pogge et al. eds., 2010).

Finally, the proponents of the model claim that access to medicines would greatly improve, since each HIF-registered innovator has strong incentives to reach out to more patients and ensure that they make optimal use of HIF covered drugs. This in turn has a significant impact on global public health.[721] However, this purported advantage in favour of greater usage of the drug will likely entail more marketing and associated expenses, an aspect that may not always be optimal from the point of view of incentivising pharmaceutical companies to spend more money on R&D and less on marketing.[722]

Owing to all of its perceived advantages, the World Health Organisation's Expert Working Group on Research and Development Financing lauded the HIF as a promising regime that could appropriately stimulate research and development for diseases of the global poor.[723] Further, both the Australian government and the European parliament have expressed a keen interest in the idea.[724]

However, the HIF model suffers from a number of significant shortcomings. Firstly, it depends on external funding through governments and other agencies,

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[721] *See id.*

[722] *See* Angell, *supra* note 69.

[723] *See* Rudolf V. Van Puymbroeck, *The Health Impact Fund: Creation and Commitment* (IGH Discussion Paper No. 6, Feb., 2010), *available at* http://www.yale.edu/macmillan/igh/files/DP6_Van_Puymbroeck.pdf.

[724] *See* Lauren Vogel, *Fund Proposed to Pay for Drugs with Greater Global Impact*, 182(5) CAN. MED. ASS'N. J. E-231 (2010); *see also* Thomas Pogge, *How the Poor can Pay for Life-saving Medicines* (Apr., 2011), http://www.guardian.co.uk/global-development/poverty-matters/2011/apr/07/how-poor-pay-for-medicines.

and will work only if such contributions flow in on a regular basis. While the monetary contribution made by various national governments is most likely to come from taxpayers in the developed countries, substantial benefits would accrue to those in developing countries.[725] It would, therefore, take a lot of political and moral pressure to ensure that developed countries continue contributing the largest portion of the fund.

Secondly, as the proponents of the model themselves acknowledge, there are several ways of gaming the model. Since funds are limited, innovators have to compete for a share of the pie, rendering the model more susceptible to rigging and inflation. Illustratively, innovators might attempt to increase the estimate of the QALYs per unit of the product sold. More problematically, given that the reward depends on the number of units sold, firms may attempt to artificially increase the number of units sold. A fairly rigorous QALY yardstick applied consistently over time along with extensive scrutiny over sales numbers should help mitigate these problems.[726] In particular, the authors of the model note that the IAC should rely on a variety of information sources to determine quantities sold, including data from pharmacies, manufacturers, wholesalers, governments and, where available, from independent data collection agencies.[727]

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[725] *See* Thomas Alured Faunce & Hitoshi Nasu, *Three Proposals for Rewarding Novel Health Technologies Benefitting People Living in Poverty: A Comparative Analysis of Prize Funds, Health Impact Funds and Cost-Effectiveness/Competitive Tender Treaty*, 1(2) PUB. HEALTH ETHICS 146 (2008).

[726] *See* Hollis, *supra* note 701, at 130.

[727] *See id.*

Thirdly, while the HIF enables drug originators to recover their manufacturing costs, it is not clear if the rewards will fully cover R&D expenses.[728] There is no explicit reimbursement for the costs of R&D of the drug, and it is unclear whether these costs will necessarily be recovered by payments made out of the HIF. The amounts that will finally be allotted to participating drug originators cannot be known in advance and depends on the fund availability at that point in time and the number of HIF registrants that are competing for the fund.[729] This uncertainty is likely to cause drug originators to continue relying on the patent system and forego the opportunity of registering with the HIF.

Fourthly, the HIF is likely to attract interest mainly with respect to neglected diseases that have negligible markets in the developed countries. As already discussed in Chapter VII, in so far as drugs for Type I or developed country diseases are concerned, companies are likely to pursue a patent-based policy, where they can sell such drugs at monopoly prices to patients in rich countries as well as to local elites in poor countries and earn much higher amounts than the funds which are likely to be received from the HIF.[730] The authors of the model themselves acknowledge that patents will continue to remain the key incentive for these drugs.

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[728] *See* Matt Peterson et. al., *A Critique in Need of Critique*, 3(2) PUB. HEALTH ETHICS 178, 183 (2010)

[729] *See* Brook K. Baker, *Skepticism about the Health Impact Fund* (Nov. 24, 2008), http://www.healthgap.org/trips/bakeronHIF.htm.

[730] *See id.*

Further, given that the HIF reward scheme depends on the number of drugs that are sold, the incentives are likely to be weak for "orphan" drugs. The authors address this concern by pointing to the potential patentability of such research, thereby suggesting that patents may offer an appropriate incentive in this context. They acknowledge that while the HIF proposal does nothing to assist in the treatment of rare diseases and conditions, it does nothing to harm them either. An alternative response might be to set aside a portion of funds only for rare diseases; however, the authors dismiss this on the ground that one of the attractive features of the HIF system is its simplicity, and any special exceptions will only complicate the model.[731]

Lastly, the model has been criticised for permitting firms to retain benefits under both the HIF fund as also the patent system, despite the alleged drawbacks of the patent system.[732] The authors of the model themselves note at several instances that the patent system is prohibitively expensive in terms of the costs of prosecuting and litigating/enforcing the patent and that their model redresses some of these inefficiencies by offering another incentive to drug makers.[733] The model permits companies to partake in the HIF rewards whilst at the same time retaining their patents and even enforcing them against infringers. All that the beneficiaries are required to do is to price the drug at a pre-determined level,

[731] *See* Hollis, *supra* note 701.

[732] *See* Baker, *supra* note 729.

[733] *See* Hollis, *supra* note 701, at 131; *see also* Hollis & Pogge, *supra* note 706, at 13.

which is likely to be much lower than what might have prevailed in a monopoly market. However, although the model might help achieve pricing that is non-monopolistic, it still engenders market concentration in favour of one firm.[734] This raises concerns about whether or not the monopolist can adequately supply the entire market and also diminishes the prospects of countries which wish to develop local manufacturing capacity by encouraging competition from local manufacturers.[735]

Hollis considers the option of open licensing to generic manufacturers, but then dismisses it, suggesting that it is likely to create complications and may not be effective outside of the U.S.[736] This cryptic dismissal of open licensing appears unconvincing. Hollis and Pogge rely instead on the ability to reduce prices by insisting that registered products be sold at prices close to the cost of manufacture. As noted earlier, this ability to regulate prices does nothing to allay fears with regards to other dangers associated with monopolistic control of a market.[737] It is also important to note that although the HIF does speak about patents, it is silent on data exclusivity, a non-patent form of market exclusivity which has been

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[734] *See* James Love, *The Health Impact Fund and Product Monopolies,* (Nov. 17, 2008), http://keionline.org/blogs/2008/11/17/health-impact-fund-monopolies.

[735] *See* Baker, *supra* note 729.

[736] *See* Aidan Hollis, *The Health Impact Fund and Price Determination*, 1(IGH Discussion Paper No. 1, Apr. 23, 2009), *available at* http://www.yale.edu/macmillan/igh/files/papers/DP1_Hollis.pdf ("While this seems intuitively attractive, generic competition is not always effective at achieving low consumer prices, particularly outside the United States. Open licensing also creates new complications related to the licensing of patents and other related know-how which may be difficult to resolve.").

[737] *See* discussion on Roche and Tamiflu in Chapter III, *supra* text accompanying notes 395-397.

extensively dealt with in Chapter III.[738] Even assuming that Hollis and Pogge were to later advocate the licensing of patents in appropriate circumstances, mere licensing on this count would not suffice, since potential generic competitors may not be able to enter the market, if the drug is also covered by other market exclusivities such as data exclusivity.

While assessing the HIF model and its various strengths and weaknesses, it is important to bear in mind that the model is a "work in progress" and that the authors have been continually updating it.[739] When the model is finally operationalised, it could well be a different version than the present one which is being assessed and may effectively redress some of its various shortcomings which have been pointed out in this Chapter.

### D. The Medical Research and Development Treaty

The Medical Research and Development Treaty (hereinafter "MRDT") requires all nations to pledge a fixed percent of their GDP towards a fund for sponsoring global pharmaceutical R&D. Priority research areas would be earmarked and any spending would generate commensurate credits counting toward a country's

[738] *See supra*, Chapter III: Data Exclusivity and Pharmaceutical Innovation.

[739] *See* Hollis & Pogge, *supra* note 706, at 11.

overall obligation.[740] Modeled on the Kyoto protocol on climate change,[741] which fosters the trading of greenhouse gas emission limits, the MRDT enables states to earn credits against their funding commitments by transferring technology to developing countries. The treaty also employs this credit mechanism to promote research on neglected Type III diseases.[742]

At the core of the MRDT treaty lies a desire to separate the costs of R&D from that of drug production and distribution. It rewards innovation directly with a prize fund continuously replenished by contributions from member states and administered by a lean secretariat.[743] The treaty, therefore, qualifies as a classic "push" mechanism to ensure that there is more funding for medical R&D and a "pull" mechanism wherein successful innovations are rewarded through prizes and the like.[744] More specifically, the treaty entails the following:[745]

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[740] *See* Andrew Farlow, *A Global Medical Research and Development Treaty: An Answer to Global health needs?* 10 (IPN Working Paper on Intellectual Property, Health and Innovation, June, 2007), *available at* http://www.policynetwork.net/health/publication/global-medical-research-and-development-treaty-answer-global-health-needs.

[741] *See* Kyoto Protocol to The United Nations Framework Convention on Climate Change, Mar. 16, 1998, 2303 U.N.T.S. 148 (*entered into force* Feb. 16, 2005); *see also* Farlow, *supra* note 740, at 10.

[742] *See* Eva Tallaksen, *World Needs Global R&D Health Treaty* (2005), http://www.scidev.net/en/news/world-needs-global-rd-health-treaty.html.

[743] *See* David J. Winters, *Expanding Global Research and Development for Neglected Diseases*, 84(5) BULL. WORLD HEALTH ORGAN. 414 (May, 2006).

[744] *See* Donald W. Light, *Advanced Market Commitments- Current Realities and Alternate Approaches*, 5 (HAI Paper Series, 03-2009/01, Mar., 2009), *available at* http://www.haiweb.org/31032009/27%20Mar%202009%20AMC%20Current%20Realities%20&%20Alternate%20Approaches%20FINAL.pdf.

1. Periodic global priority assessments, including estimates of funding for R&D.

2. Norms and mechanisms to ensure sustainable financing for R&D.

3. Measures to facilitate, encourage, and stimulate new incentive schemes for R&D (such as medical innovation inducement prizes, advanced market commitments, openness dividends, and other new innovative approaches).

4. Global norms and best practices to facilitate access to government funded research.

5. Measures to improve the delivery of and access to health products.

6. Mechanisms to enhance R&D and innovation capabilities in developing countries.

7. Measures to achieve compliance with appropriate ethical standards for medical research.

The treaty originators propose that it ought to supplement or replace trade agreements such as the TRIPS agreement in so far as pharmaceutical drugs are concerned.[746]

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[745] *See* PROPOSAL BY BANGLADESH, BARBADOS, BOLIVIA AND SURINAME: PROPOSAL FOR WHO DISCUSSIONS ON A BIOMEDICAL R&D TREATY 2-3 (Apr. 15, 2009), *available at* http://www.who.int/phi/Bangladesh_Barbados_Bolivia_Suriname_R_DTreaty.pdf [hereinafter BANGLADESH PROPOSAL].

[746] *See* Farlow, *supra* note 740, at 11.

This treaty has its fair share of supporters and detractors. It was heavily promoted during the deliberations of the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) of the WHO between 2004 and 2006.[747] It was further discussed in 2009 as part of a proposal put before the WHO by a group of researchers from Bangladesh, Barbados, Bolivia and Suriname.[748] Unfortunately, it was labelled as untenable by a WHO committee which was tasked with identifying the most promising proposals for inducing public health related innovation.[749] Andrew Farlow criticises the treaty for the absence of any explanation of how different modes and funding of R&D would coexist, how the production side of the proposal would work and on how non-patent based R&D will be efficiently appropriated.[750]

As with the earlier discussed model which was based on public funding of clinical trials, the key challenge for such an alternative regime would be in terms of procuring sustainable funding from the various member states. Further, given the entrenchment of various interests in a post-TRIPS era and the gradual ratcheting

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[747] *See* BANGLADESH PROPOSAL, *supra* note 745.

[748] *See* BANGLADESH PROPOSAL, *supra* note 745 at 2-3.

[749] *See* International Centre for Trade and Sustainable Development, *WHO Tackles Intellectual Property, R&D Treaty*, 13(19) BRIDGES WEEKLY TRADE NEWS DIGEST (May, 2009) http://ictsd.org/i/news/bridgesweekly/47396.

[750] *See* Farlow, *supra* note 740, at 5.

up of harmonized IP standards by free trade agreements (hereinafter "FTAs"), the prospects of amending TRIPS or overriding it by another treaty appear bleak.[751]

### E. The Advanced Market Commitment (AMC) Regime

An Advanced Market Commitment (hereinafter "AMC") or an Advanced Purchase Contract (hereinafter "APC") is primarily aimed at providing sufficient "market" incentives to foster the creation of new drugs, particularly vaccines, for Type III neglected diseases that disproportionately afflict low income countries.[752] It is also aimed at speeding up access to new vaccines in poor countries, which often experience a delay in procuring such vaccines, owing to high prices.[753]

In essence, AMC's are commitments made by governments and non-profit organizations to offer a fixed price to a drug originator who comes up with a specified new drug.[754] The underlying idea is that donors would match the revenues that drug originators earn from developing medicines for affluent markets, such that they have an equivalent incentive when working on cures for

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[751] *See id.; see also* J.A. DiMasi & H. G. Grabowski, *Should the Patent System for New Medicines Be Abolished?*, 82(5) CLIN. PHARMACOL THER. 488 (Nov., 2007).

[752] *See* Ernst R. Berndt & John A. Hurvitz, *Vaccine Advance-Purchase Agreements for Low-Income Countries: Practical Issues*, 24(3) HEALTH AFF. 653, 654 (2005).

[753] *See* Light, *supra* note 744, at 1.

[754] *See* Stephen Maurer, *When Patents Fail: Finding New Drugs for the Developing World*, 3 (International Conference on Pharmaceutical Innovation, Taipei, China, May 27, 2005), *available at* http://gspp.berkeley.edu/iths/Maurer_WhenPatentsFail.pdf.

neglected diseases. These instruments have been particularly recommended for vaccine development.[755]

A financially credible program sponsor or coalition of sponsors would typically sign a contract underwriting a guaranteed price for the supplier. Poor countries would decide whether to buy a product at a low and affordable price (say, U.S. $1 per treatment), and sponsors would guarantee to top-up to a guaranteed price (say, U.S. $15 per treatment) – thus, providing market returns for the developer which are comparable to other mainstream drugs. Once the full number of treatments is purchased at the guaranteed price, the supplier commits to selling further treatments at a low affordable price.[756] By guaranteeing a certain amount of purchases at a fixed sum, the AMC reduces economic uncertainty for pharmaceutical firms and offers more confidence to investors. Such an incentive is likely to be effective for disease cures which fail to be incentivised by the current patent regime, such as Type III neglected diseases.[757]

However, for the model to work effectively, parties must enter into a binding contract. Illustratively, the case of the anti-malarial drug, Coartem exposed certain weaknesses in this regard. A Memorandum of Understanding (hereinafter "MoU")

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[755] *See* Berndt & Hurvitz, *supra* note 752, at 654.

[756] *See* Michael Kremer et al., *Briefing Note on Advance Purchase Commitments*, 19 (DFID Briefing Paper, May, 2005), *available at* http://www.who.int/intellectualproperty/submissions/MichealKremerKTW_CIPIH_submit_2.pdf.

[757] *See id.* at 1.

had been signed between Novartis and the WHO in 2001, under which Novartis agreed to provide Coartem at cost, for 10 years to the public agencies of malaria-endemic countries channelled through the WHO. However in 2005, Novartis announced that production would fall nearly 1 million doses short of the 2.4 million promised for 2005.[758]

This model was first advocated by Michael Kremer, who labelled it as an Advanced Purchase Agreement or Commitment (hereinafter "APC").[759] Later, it was renamed as an Advanced Market Commitment.[760] Donald Light argues that APC is a more accurate term, since the core idea of this model is to compensate a firm upto an amount equalling the lifetime average revenue for a new drug that sells reasonably well in the developed country markets.[761] In other words, since the model relates to a single firm (and a commitment to purchase drugs at fixed prices from that firm) and not an entire disease market involving several firms, it is more

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[758] *See id.* at 22.

[759] The 2006 report of Commission on Intellectual Property Rights, Innovation, and Public Health (CIPIH) also refers to the idea as an APC. *See* RACHEL GLENNERSTER & MICHAEL KREMER, STRONG MEDICINE: CREATING INCENTIVES FOR PHARMACEUTICAL RESEARCH ON NEGLECTED DISEASES (2004); *see also* WHO COMMISSION ON INTELLECTUAL PROPERTY RIGHTS, INNOVATION AND PUBLIC HEALTH, PUBLIC HEALTH, INNOVATION AND INTELLECTUAL PROPERTY RIGHTS, REPORT OF THE COMMISSION ON INTELLECTUAL PROPERTY RIGHTS (2006), *available at* http://www.who.int/intellectualproperty/documents/thereport/ENPublicHealthReport.pdf.

[760] *See* RUTH LEVINE, MICHAEL KREMER & ALICE ALBRIGHT, CENTER FOR GLOBAL DEVELOPMENT, MAKING MARKETS FOR VACCINES: IDEAS TO ACTION (2005), *available at* http://www.cgdev.org/doc/books/vaccine/MakingMarkets-complete.pdf.

[761] *See* Light, *supra* note 744, at 5-6.

appropriate to label it as an APC.[762] For the purposes of this thesis, I use the terms APC and AMC interchangeably.

The AMC concept has been theorised and implemented with many variations around the core idea, of donors committing, in advance of product development, to finance the purchase of drugs for low-income countries, at a price that is specified in advance. While assessing the merits of such a model, I focus on the core idea outlined above.

Firstly, a key problem with an APC, when compared with other incentive proposals such as the HIF, is that it works effectively only in situations where the goals are predetermined and the rewards worked out *ex ante*.

Secondly, the AMC design tends to pit research teams against one another and encourages the retention of new discoveries as trade secrets, as opposed to a collaborative approach, where discoveries are shared between groups of researchers.[763] The idea that co-operative and not competitive research is necessary to discover vaccines and cures for neglected diseases such as malaria and

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[762] *See* GLENNERSTER & KREMER, *supra* note 634; *see also* Michael Kremer et al., *Creating Markets for Vaccines* (2006), *available at* http://www.economics.harvard.edu/faculty/kremer/files/innovationsFinal.pdf; *see also* James Love & Tim Hubbard, *The Big Idea: Prizes to Stimulate R&D for New Medicines*, 82(3) CHIC. KENT L. REV. 1519, 1544 (2007); *see also* Fisher & Syed, *supra* note 443, at 22.

[763] This situation is no different than what prevails today in a patenting context.

HIV/AIDS is slowly gaining traction.[764] The AMC, by contrast, encourages competitive research, and motivates teams to compete against one another for a very large prize.

Thirdly, Light notes that certain desirable flexibilities that had been incorporated in earlier AMC models have been done away, such as patent buyouts and licensing.[765] He argues that the current layout of the AMC appears to be strongly protective of property rights, despite its dedication to reducing disease burden and improving access in countries that suffer from patent barriers to medicines.[766]

Fourthly, the AMC model has a major drawback in that, once a commitment has been made, governments cannot opt to purchase a better drug or vaccine that is discovered at the same time or shortly afterwards.[767]

Lastly, since prices are fixed, an improved product cannot earn more revenue than the first generation product. For this reason, the first generation inventor has no incentive to improve its own product or make its technology

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[764] *See* Bill & Melinda Gates Foundation, *The Road to an HIV Vaccine* (2006), http://www.gatesfoundation.org/nr/public/media/annualreports/annualreport06/AR2006GH2.html.

[765] *See* Light, *supra* note 744, at (i).

[766] *See id.* at 10.

[767] *See* Berndt & Hurvitz, *supra* note 752, at 657-658.

available to others. Instead, its best strategy is to block the better product until, the sponsor agrees to pay an additional, "monopolysise" bonus.[768]

Notwithstanding the deficiencies of the AMC, this model has the potential to drive a greater amount of R&D into vaccines for neglected diseases. Further, a key advantage for donors is that no costs are incurred, unless and until a drug is successfully developed. Moreover, APC's can be implemented alongside existing incentives for pharmaceutical innovation.[769] However, given that it works only within limited contexts such as vaccines for neglected diseases, it cannot substitute for the more broad-based investment regime proposed in this thesis.

### F. Collaborative Innovation Commons

The term "commons" generally refers to a resource shared by a group of people.[770] It is used in this thesis to connote the absence of exclusionary legal norms in relation to an information resource.[771] An "innovation commons" could be defined very broadly as an open and free platform where pertinent information relating to a certain technological domain is made available. The platform and the terms of engagement aim to foster an open collaboration between the various users of the

[768] *See* Maurer, *supra* note 754, at 8.

[769] *See* Berndt & Hurvitz, *supra* note 752, at 654-655.

[770] *See* Charlotte Hess & Elinor Ostrom, *Introduction: An Overview of the Knowledge Commons*, *in* UNDERSTANDING KNOWLEDGE AS A COMMONS 4-26 (2007).

[771] *See* John Cahir, *The Withering Away of Property: The Rise of the Internet Information Commons*, 24 OX. J. LEGAL STUDIES 4, 619-641 (2004).

platform so as to facilitate the creation of new ideas and products building upon information hosted by the platform.[772] I take the creative liberty of labelling this as a "collaborative innovation commons."

The core philosophy underlying such a model derives from the wisdom that the development of a "commons" of freely accessible knowledge and a collaboration between various participants is likely to yield a much higher rate of innovation, than a closed framework where knowledge is locked away through IP rights and made accessible to only a few participants in accordance with the wishes of the IP owner.[773] Keeping with this philosophy, most innovation commons models are likely to prohibit the enforcement of patents covering any aspect of the information resource that is part of the commons, rather the information content underlying such patents ought to be free for all to use.[774]

The term "collaborative innovation commons" is wide enough to cover a variety of innovation models currently in vogue today, including free and open source software (hereinafter "FOSS"), the most popular of the breed. At its very core, a FOSS framework entails the free availability of software source code, such

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[772] *See* ERIC VON HIPPEL, DEMOCRATIZING INNOVATION (2005).

[773] *See* Andrea Bonaccorsi & Cristina Rossi, *Why Open Source Software can Succeed* 2 (LEM Working Paper No. 15, 2002), http://papers.ssrn.com/sol3/papers.cfm?abstract_id=348301.

[774] The President of the Center for Global Development calls for a 'global commons' in which the best minds work together for "a global social contract." CENTER FOR GLOBAL DEVELOPMENT, MAKING MARKETS FOR VACCINES: IDEAS INTO ACTION 115 (2005), *available at* http://www.cgdev.org/doc/books/vaccine/MakingMarkets-complete.pdf.

that it can be improved upon by any interested member of the public. However, the typical terms of engagement for most such initiatives are likely to stipulate that anyone who benefits from access to the source code must plough back their improvements to the group that made the software available in the first place.[775] The terms of engagement are laid out in copyright licensing terms, since software is entitled to automatic protection as copyrightable work in most global jurisdictions.[776]

One of the most popular licenses is the GNU[777] General Public License (hereinafter "GPL"), which allows any user to run, copy, study, redistribute, modify and improve software licensed under its terms. If a participant modifies a GPL software, she would have to license the modified software under terms no less restrictive than the GPL. In this way, GPL software begets GPL software. Linux is an example of software distributed under the GPL.[778] Other well-known examples of

[775] *See* Bonaccorsi & Rossi, *supra* note 773.

[776] For example, in many jurisdictions such as the U.S., computer programs are treated as literary works. Copyright Act 17 U.S.C. § 101 (1980); *see also* § 2(o) r/w § 13, Indian Copyright Act, 1957 (providing that computer programs are copyrightable as literary works in India).

[777] The GNU project was launched in 1984 and is aimed at developing the GNU operating system, a Unix-like operating system, which is free software. "Unix-like operating systems are built from a software collection of applications, libraries, and developer tools—plus a program to allocate resources and talk to the hardware, known as a kernel." *GNU Operating System,* http://www.gnu.org/ (last visited Sept. 30, 2011).

[778] *See* Erik J. Heels, *How and Why to try Open Source Software*, 29 LAW PRAC. MGMT. 43, 44 (2003).

open source software are the Apache server software, the Perl programming language and the Mozilla web browser.[779]

As is obvious, the key advantage of FOSS is that from a consumers' perspective, it is significantly cheaper than proprietary versions.[780] Many also argue that given the nature of the collaborative and continuous input received on the code from a wide variety of experts, the software is likely to be superior to proprietary versions.[781] In particular, it is argued that such software is often more reliable and less prone to technical glitches.[782] However, there have been several criticisms ranging from the fact that that FOSS is not really free of cost (while there may be no costs to be incurred upfront; there are often unseen or unanticipated costs for implementation, administration and support)[783], to the fact that such software may contain unauthorised intellectual property belonging to third parties.[784]

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[779] *See* Georg von Krogh & Eric von Hippel, *Special Issue on Open Source Software Development*, 32 RESEARCH POLICY 1149 (2003).

[780] *See* Carla Michler, *The Procurement Decision-"Open" or "Closed" Source Software?*, 10 DEAKIN L. REV. 261 (2005).

[781] *See id.*

[782] *See* Bonaccorsi & Rossi, *supra* note 773, at 20 (noting that in fact, one of the main advantages of Linux over Windows is its resistance to crashes which can be measured in months and years rather than days or weeks).

[783] *See* Thomas Warger, *The Open Source Movement*, EDUCASE QTRLY. 18, 20 (May, 2002); *see also* Codrin Marius Teiu, *Review on Open Source Software*, 3 (Working Paper, Oct. 28, 2010) http://papers.ssrn.com/sol3/papers.cfm?abstract_id=1703561.

[784]*See* Kirk D. Rowe, *Why Pay for What's Free? Minimising the Patent Threat to Free Open Source Software*, 7 J. MARSHALL REV. INTELL. PROP. L. 595, 601 (2008); *see also* Jason Williams et al., *The Advantages of Adopting Open Source Software*, *in* EXPANDING CHOICE: MOVING TO LINUX AND OPEN SOURCE WITH NOVELL OPEN ENTERPRISE SERVER (2005); *see also* PARLIAMENTARY OFFICE OF SCIENCE AND

Notwithstanding the various critiques, the FOSS movement has inspired several other "open" collaborative initiatives such as Wikipedia, a free online encyclopaedia that is open to editing by any interested member of the public.[785] It now boasts of innumerable contributors who share their knowledge and scholarship on almost every area of human knowledge, without direct compensation or academic credit and with the constant risk of having their work altered.[786] The FOSS model has also been adopted in other technological domains such as biotechnology[787] and pharmaceuticals.[788] Illustratively, the Open Source Drug Discovery (hereinafter "OSDD"), an initiative by the CSIR deploys an online social networking platform to leverage the expertise of scientists, students and other interested experts to arrive at a potential cure for tuberculosis (TB).[789] Given

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TECHNOLOGY (U.K.), OPEN SOURCE SOFTWARE (POST Note No. 242, Jun. 2005), *available at* http://www.parliament.uk/documents/post/postpn242.pdf.

[785] *See* Andrew George, *Avoiding Tragedy in the Wiki- Commons* 2 (Working Paper, 2008), http://papers.ssrn.com/sol3/papers.cfm?abstract_id=975096.

[786] *See id.*

[787] For instance, the BiOS initiative is aimed at fostering decentralized, cooperative innovation in the application of biological technologies, through the merging of: intellectual property, informatics, analysis, innovation system structural reform and cooperative open access technology development activities. Biological Innovation for Open Society, *BiOS Initiative*, http://www.bios.net/daisy/bios/bios.html (last visited Sept. 30, 2011).

[788] *See* Stephen M. Maurer et al., *Finding Cures for Tropical Diseases: Is Open Source the Answer?* (Dec., 2004), 1(3) PLOS MED.

[789] *See* Open Source Drug Discovery*, About Us*, http://www.osdd.net/about-us (last visited Sept. 30, 2011).

the "open" and "free" nature of the technological platform, the price of any resulting drug is likely to be low.[790]

The participants in the OSDD consist of students, scientists, researchers, academics, institutions, corporations and others committed to the ideology of discovering drugs in an open collaborative mode. The nature of the online model is thus:

1. The process of drug discovery is divided into problems, which are posted on the online platform. Any participant is welcome to solve any specific problem.

2. A "micro-attribution system" operates as an incentive for people to contribute. This system is based on a peer-review of individual contributions, based on which such contributors earn rewards. Each activity and problem solution has a specific set of points associated with it.

3. Based on the points accrued by the contributors, they are awarded four levels of membership cards (Blue, Silver, Gold and Platinum) and each type of card entails a certain sets of rights, privileges and responsibilities in the entire process.[791] Some contributions even entail financial rewards.

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[790] *See* Open Source Drug Discovery, *What Is OSDD*, http://www.osdd.net/what-is-osdd (last visited Sept. 30, 2011).

[791] *See* Open Source Drug Discovery, *How does OSDD Work*, http://www.osdd.net/how-does-osdd-work (last visited Sept. 30, 2011).

As the OSDD website states, "[t]he open source drug discovery model...exploits the system of monetary and non-monetary rewards that is already part of the scientific establishment—using the prospects of scientific progress, career advancement, and humanitarianism to engage biomedical researchers."[792]

Given that this model fosters collaboration among a diverse set of skilled researchers across the world, one can expect it to generate potential leads.[793] A key challenge for the model is the classic "free-rider" problem, wherein employees of a private pharmaceutical corporation can sign up to the network under a pseudonym, grab an idea that is close to fruition and take it to the corporation that they work for to have it subsequently developed therein. The corporation could then claim that it had both discovered and developed the idea by itself. As of now, the OSDD model does not appear to have any effective means of preventing such instances of fraud and false credit, notwithstanding the contractual terms that each of the participants in the online platform have agreed to abide by.[794] However, Zakir Thomas, Project Director of the OSDD, opines that this threat is more academic than real, as the prospects of private firms wanting to steal ideas from the platform is

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[792] *See id.*

[793] Telephonic Interview with Zakir Thomas, Project Director of the OSDD (Apr. 25, 2011) (stating that the OSDD platform has not generated its own leads yet; however, it has picked up two potential leads from government institutions, namely CDRI (Central Drug Research Institute) and NII (National Institute of Immunology) and is now in the process of optimising these leads with the help of two private firms with expertise in this area); *see also* Jacob B. Koshy, *CSIR in Talks for Clinical Trials on Two Open-source Molecules*, (Mar. 24, 2011), http://www.livemint.com/2011/03/23224801/CSIR-in-talks-for-clinical-tri.html?atype=tp .

[794] *See* Rowe, *supra* note 784, at 608.

rather remote. He notes that, "In many ways, the OSDD platform owes its genesis to the fact that neglected diseases have been neglected by leading pharmaceutical firms. Expecting such leading firms to steal ideas from the platform and spend money developing them, when the markets for such drugs are not as profitable, is far-fetched."[795]

Secondly, one is not certain as to how the said molecule, once identified would be developed. And this is the biggest challenge for OSDD or any similar model premised on an open and collaborative framework for pharmaceutical drug development. The OSDD team expects the Indian government to fund the entire development process, including trials.[796] It is pertinent to note in this connection that the developmental costs may not only relate to one molecule, but several potential lead molecules, which may fail during trials. As already discussed in Chapter I, the percentage of drug candidate failures, as a lead moves through the various regulatory phases (pre-clinical and the various clinical stages), is significant. Typically, less than 1% of the compounds examined in the pre-clinical period make it to human testing.[797] Of the compounds that finally make it to human

[795] *See* Interview with Zakir Thomas, *supra* note 793.

[796] *See id.* ("We are not really worried about securing funding for the development of the lead, as the government will continue to support this project. Rather, our main concern is in locating the right lead that would yield the desired results.").

[797] *See* Grabowski, *supra* note 42.

testing, only 19% of them survive the development process and gain FDA approval.[798]

This essentially means that pharmaceutical companies cannot bank on a single lead, but have to test several of them, since the risk of failure prior to final assessment by the FDA is significant.[799] Given this high risk framework, the government will necessarily have to fund the entirety of the process, where several leads are tested. Even assuming that the government covers all the expenses relating to the current work of the OSDD project, it is not clear if such funding will be available for future drugs.

Alternatively, the drug development expenses mentioned above could be borne by a private entity, such as a firm with expertise in drug development. However, private firms are unlikely to invest such significant sums of money, without the guarantee of sound financial returns. And this brings us back to the investment protection regime proposed in this paper, premised on exclusivity or alternatively, on compensatory liability.

### G. Concluding Observations

[798] *See* DiMasi et al., *supra* note 43.

[799] *See* Grabowski, *supra* note 42.

It is important to bear in mind that unlike patent and data exclusivity regimes, that have operated through statutory regimes for several decades and been interpreted through myriad case law, the various alternative incentive models discussed in this Chapter are yet to be tested rigorously through the experiential lens of the law. This important limitation must be borne in mind, while assessing these alternative models. In particular, it bears noting that a large majority of these models admit of several variations. The HIF is an excellent illustration of this, with the advocates of the model claiming that it is a work in progress.[800]

A key limitation of most alternative models discussed in this Chapter is that they are better suited towards cures for Type III diseases drugs, and are incapable of substituting the patent and data exclusivity regimes to yield a more optimal fostering of R&D incentives for Type I diseases drugs. As a comprehensive innovation inducing regime for Type I diseases, the investment protection regime proposed by this thesis appears more optimal, as it can effectively substitute the data exclusivity and patent regimes (to some extent) for a wide range of drugs. The key advantage of this regime lies in the fact that it closely aligns with principles of free market competition and helps foster pharmaceutical innovation with the least amount of external support from outside agencies, whether through funding or otherwise.

[800] *See* Hollis & Pogge, *supra* note 706, at 11.

Secondly, by rewarding the drug maker proportionately to the global health impact achieved by the drug, this regime spurs the diversion of R&D resources from mere "me-too" versions to new drugs with significant health impact.

Thirdly, the investment protection regime addresses excessive pricing concerns to some extent by its inbuilt compulsory licensing or compensatory liability mechanism.

The key disadvantage of the proposed regime is that it is likely to incentivise only those drugs that command high consumer prices i.e. drugs for developed country diseases. Given the steady decrease in the number of new drugs over the last several years, it is desirable to engender as many incentive mechanisms as possible. Therefore, it is advisable that, along with the models advocated in this thesis, a range and diversity of other models including APC's, HIF and collaborative innovation commons be pursued for encouraging global pharmaceutical innovation.

The vast majority of drugs today cater to developed country diseases and are attributable to private firms.[801] Consequently, the investment protection regime proposed in this thesis focuses on market incentives for private firms to pursue cures for such diseases. The proposed incentives take the form of legal protection against competitors who manufacture drugs that are similar to that of the drug originator.

[801] *See* Friedman, *supra* note 604.

## CONCLUSION

While critics have arraigned the patent system for being premised on an unproven innovation incentive foundation, they readily concede that pharmaceutical drugs are an exception. The logic underlying this concession is that patents are necessary to support the significant investments required to introduce a drug into the market. This thesis demonstrates that if the key concern is one of investment protection, the patent regime is sub-optimal, in that it only protects certain kinds of investments i.e. investments on inventions that qualify as "new" and "inventive". Further, patents offer a uniform period of protection to all inventions, without any consideration for the actual investment per invention or its consequent social value.

Rather than attempting to shoehorn an investment protection rationale into the existing patent regime, I argue that one must evolve an investment protection regime. The formulation of such a regime relieves the patent regime from the task of investment protection, a task for which it is ill suited. Consequently, countries need not unduly lower their patentability thresholds in order to protect pharmaceutical investments.

While the "data exclusivity" regime aims to protect investments in drug development, it suffers from certain shortcomings such as a uniform period of protection for all drugs and a failure to consider the extensive costs associated with

the drug discovery phase. I recommend a more comprehensive regime to reward investment in a proportionate manner. The model asks for drug originators to submit their actual costs of drug discovery and development, and compensates them only to the extent of such costs, along with an appropriate rate of return on investment that would, *inter alia,* depend upon the health impact of the drug in question. By rewarding the drug originator in proportion to the health impact of the particular drug, the proposed investment protection regime helps shift the focus of R&D efforts from "me-too" versions to truly inventive drugs with significant social value.

Further, by permitting drug originators to include the costs incurred in relation to failed leads per target or even failed targets per disease, the regime incentivises greater risk-taking, an aspect that is particularly important, given the increasing uncertainty associated with drug development today. The proposed regime delinks investment protection from "data reliance" and treats the issue as one of market exclusivity aimed at preventing free-riders. An incidental advantage of the regime is that, over a period of time, one is likely to get a more accurate estimate of the average costs for drug discovery and development. However, a key limitation is that the proposed regime may not adequately incentivise the creation of drugs for "developing country" diseases or Type III diseases.

Given that legal exclusivities often engender monopoly markets with excessive pricing, this thesis recommends the institution of compulsory licensing

norms to foster more competition in the market and, thereby, lower prices. As an alternative, I propose a more broad based compensatory liability model based on cost sharing, where any follow-on entrant is free to manufacture the drug, upon the payment of reasonable compensation. I offer a novel framework for calculating such reasonable compensation that is more optimal than existing models. This model is likely to be more effective and advantageous in those countries that already have drug-manufacturing capabilities and who wish to keep drug prices low.

I also consider the relevance of patents to pharmaceutical innovation. Although the issue of whether or not patents foster innovation is empirically inconclusive, I argue that, in view of the existence of the patent system for several centuries, one ought not to abolish the patent system without more compelling evidence of its impotence. More importantly, TRIPS does not afford member states the luxury to dispense with the patent regime. However, given that the concerns of investment protection are met through a separate regime, I argue that countries are free to institute higher patent thresholds without being excessively concerned about the potential adverse impact on pharmaceutical investment.

Lastly, it bears noting that the proposed investment protection regime works well in the context of pharmaceutical innovation. Given that the creation of new drugs is closely associated with a structured and determinable regulatory process, it is relatively simpler to measure the value of output and compute

investments that require to be protected. It may not be easy to apply a similar model to other areas of technology that do not possess a similar regulatory regime to filter output.

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